ABSTRACTS OF WORLD MEDICINE

VOL. 18 No. 4 OCTOBER, 1955

Pathology

EXPERIMENTAL PATHOLOGY

908. **The Significance of Reflexes in the Development of Disease.** (Значение рефлексов в развитии болезней) A. D. ADO. *Архив Патологии* [*Arkh. Patol.*] **17**, 3–10, Jan.–March, 1955. 12 refs.

There has been a tendency within recent years for some Soviet authors to ascribe the origin of all pathological reflexes, conditioned and unconditioned, to an abnormal stimulation of the receptor ends of the reflex arc. The author criticizes this concept on the basis of evidence obtained from experiments with the toxin of *Clostridium botulinum* and the viruses of influenza and poliomyelitis. This evidence shows that the main effect of the pathological agents in these cases is central. He does not deny that some pathological agents act mainly upon receptors and others upon effectors, but points out that there seems to be no uniform or universal pattern in the initiation of pathological reflex mechanisms. *L. Crome*

909. **Studies on Entry and Egress of Poliomyelitic Infection. VIII. The Relation of Viremia to Invasion of the Central Nervous System**
H. K. FABER and L. DONG. *Journal of Experimental Medicine* [*J. exp. Med.*] **101**, 383–389, April 1, 1955. 19 refs.

The recent discovery that a viraemic phase occurs in poliomyelitis has made it necessary to reconsider the blood as a possible route of invasion of the central nervous system (C.N.S.) in addition to axonal transmission of the virus through the peripheral nerves. In this paper from Stanford University School of Medicine, San Francisco, the authors describe the results of injecting three groups each of 4 cynomolgus monkeys with suspensions containing approximately 6,000 PD_{50} of the Wis'45 strain (Type 1) of poliomyelitis virus, intravenously in one group and into the carotid and vertebral arteries respectively in the other two.

In the intravenously inoculated group no symptoms developed in any of the monkeys and no lesions were found in the C.N.S. at 3 or 5 days after inoculation. Of the animals inoculated by way of the carotid artery no symptoms developed in 3, although some traces of perivascular and parenchymal infiltration in the rostral region were observed in one of these; the fourth developed bulbar paralysis on the 6th day and extensive lesions were found throughout the brain-stem and cord, the initial paralysis indicating that the site of entry of the virus into the C.N.S. had been in the pons and medulla. Of those given the injection into the vertebral artery, no symptoms had developed in 2 animals killed on the 3rd and 5th days respectively after inoculation; the third died on the 4th day, and the fourth developed paralysis on the 8th day. All were found to have extensive involvement of the regions supplied by the vertebral artery, that is, the neuronal regions of high susceptibility. Involvement was greatest in the cord, but invasion of all the various affected areas appeared to be simultaneous. No evidence of primary invasion from the blood through a region of increased vascular permeability, such as the area postrema, was found.

After nerve-borne entry into the C.N.S. the initial localization of lesions is different from that resulting from viraemia. The authors consider that the signs following invasion of the C.N.S. by way of the peripheral nerves provide a better correlation with the clinical picture at the onset of infection than do those consequent on infection via the blood stream. *A. Ackroyd*

910. **Histochemical Studies of Early Experimental Myocardial Infarction. Periodic Acid–Schiff Method**
H. O. YOKOYAMA, R. B. JENNINGS, G. F. CLABAUGH, and W. B. WARTMAN. *Archives of Pathology* [*Arch. Path. (Chicago)*] **59**, 347–354, March, 1955. 7 figs., 32 refs.

In a study carried out at the Northwestern University Medical School, Chicago, the authors determined the changes in glycogen distribution in myocardial fibres, as shown by periodic-acid–Schiff (P.A.S.) staining, in myocardial infarction produced experimentally in dogs by ligating a coronary artery.

They found that soon after ligation there was loss of glycogen from individual fibres and groups of fibres, the contrast between ischaemic and normal areas being marked after one hour. Fibres showing loss of glycogen also showed disorganization, which was visible in sections stained with haematoxylin and eosin, especially in freeze-dried material, in which it was exaggerated by ice-crystal artefacts. Several days after ligation, when necrotic muscle was being replaced by granulation tissue, the muscle around the infarcted area showed an increased glycogen content.

In some areas ischaemic muscle fibres showed intense and diffuse P.A.S. staining, which was unaffected by amylase and was therefore not due to glycogen. This change appeared within one or 2 hours, was marked at 24 hours, and lasted for 14 to 28 days. In further experiments excised heart muscle was allowed to auto-

lyse at 27° C. before fixation, when it showed loss of glycogen content, this loss beginning after one hour and being almost complete in 5 hours. Diffuse amylase-resistant P.A.S. staining was also observed.

M. C. Berenbaum

911. **Antibodies Elicited by Cancer in Patients**
J. B. GRAHAM and R. M. GRAHAM. *Cancer* [*Cancer* (N.Y.)] **8**, 409–416, March–April, 1955. 34 refs.

The authors review the literature dealing with systemic resistance to tumour growth, and conclude that there is presumptive evidence in favour of an immune response to spontaneous tumours during the early part of their growth which, however, usually disappears later. In an investigation carried out at Massachusetts General Hospital, Boston, they prepared a water-soluble, saline-insoluble extract of malignant tissue from tumours removed from the vulva, cervix or corpus uteri, and ovary of 48 patients at operation. This extract, which was believed to contain the deoxyribonucleoprotein, was tested as an antigen against the patients' serum in a complement-fixation reaction. In 12 out of the 48 cases serum titres of 1 in 16 to 1 in 128 were obtained. It was noted that no such antibodies were detected in patients with far-advanced neoplastic lesions.

M. H. Salaman

HAEMATOLOGY

912. **The Relation of the ABO Blood Groups to Rh Immunization in Pregnancy. With Special Reference to the A_1 A_2 Subgroups.** [In English]
H. HEISTO. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **36**, 257–262, 1955. 8 refs.

In comparison with the normal distribution of blood groups in Norway as determined by Hartmann and Lundevall, a series of 745 rhesus-negative women iso-immunized by pregnancy only contained a smaller proportion of Group O and higher proportions of all the other groups. This confirms the experience of workers in other countries, but contrary to the findings of Wiener (*Blood*, 1953, **8**, 1024) no significant difference from the normal population could be demonstrated in the A_1:A_2 ratio.

Among 507 of the husbands of the women tested the frequency of Group O was higher and of the other groups lower than normal. But again no significant difference could be shown between the A_1:A_2 ratio in this group and that in the normal population. *John Murray*

913. **A New Micro-method for the L.E. Cell Phenomenon**
I. SCHULTZ, J. BAUM, and M. ZIFF. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **88**, 300–302, Feb., 1955. 1 fig., 4 refs.

The authors, from the Bellevue Medical Center, New York, describe a new technique for demonstrating the lupus erythematosus (L.E.) cell phenomenon. This consists in exposing a film of normal living polymorphonuclear leucocytes to serum suspected of containing the L.E. factor. This is performed on a glass slide, which is incubated for one hour at 37° C. and then dried and stained. The leucocyte film is prepared by allowing 3 drops of normal blood to clot on a glass slide for 20 minutes at 37° C. in a damp chamber; the clot is then washed off with saline. The film which remains consists almost entirely of polymorphs.

This method was found to compare favourably with the 2-hour clot technique, often giving a clear positive when the result of the clot technique was equivocal. It is claimed that all the features of the L.E. cell phenomenon may be observed and the likelihood of false positive results is reduced. *E. G. Rees*

914. **Thromboplastin and Russell Viper Venom. Investigation of the Activation of Prothrombin**
A. WENCKERT and I. M. NILSSON. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **7**, Suppl. 15, 1–97, 1955. 49 figs., bibliography.

915. **The Differential Thrombocyte Count in Cancer.** (Тромбоцитарная формула при раке)
V. A. DROZDOVA. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **33**, 32–38, April, 1955. 2 refs.

The author suggests that in the diagnosis of cases of cancer determination of the total and differential thrombocyte counts may be of considerable assistance. The thrombocytes are classified in accordance with the method of Jurgens and Graupner as young, mature, old, degenerate, and irritative forms according to their size, shape, staining properties, and other morphological characteristics. (These criteria are set out in detail in a table.)

On the blood of 132 patients thrombocyte counts were carried out 213 times, more than one count being performed in 62 cases. Of these patients, 76 were suffering from cancer (11 from cancer of the lung, 4 of the oesophagus, 48 of the gastrointestinal tract, 3 of the pancreas, 4 of the liver, 2 of the breast, and one each of the thyroid, prostate, uterus, and ovary). Of the remaining patients, 6 had tumours of other types, such as sarcoma, hypernephroma, epithelioma, neuroblastoma, and myeloma, while 50 had various other diseases not associated with cancer, the clinical material in this investigation thus being comprehensive.

In the cases of cancer the number of thrombocytes averaged 75 per 1,000 erythrocytes. There was a marked tendency to agglutination, 6% were of large size, and 2% were vacuolated. On the average more than half were old forms (whereas in healthy persons 60 to 95% were mature, as against an average of 34·8% in patients with cancer), and in only 2 cases were fewer than 30% of thrombocytes classed as old. In successive counts on the same patient the percentage of old forms increased with the duration of the disease. In patients with sarcoma and hypernephroma the findings were analogous to those in the patients with carcinoma.

In 97% of the cases diagnosis by means of radiological and histological findings at operation or post mortem

confirmed that suggested by the thrombocyte count, and only in 3% did the latter not indicate the presence of cancer. It is pointed out, however, that cases of infective hepatitis often give misleading counts; for example, in one case of this condition 71% of the platelets were of the old type, but a further count 3 weeks later showed a fall in this figure to 31%, and a still later count showed only 26%, whereas in cancer there is a tendency for the percentage count of old thrombocytes to rise. The same phenomenon was observed in a case of atypical pneumonia with severe haemoptysis; and in fact many patients with severe haemorrhage give counts suggestive of cancer. In the author's opinion the elements of the thrombocyte system are more sensitive to biological changes in the organism than other formed elements of the blood, and changes in them appear earlier and last longer than do other morphological changes in the blood. *L. Firman-Edwards*

CHEMICAL PATHOLOGY

916. **Serum and Liver Lipids in Patients with and without Liver Disease**

B. H. Billing, R. M. Haslam, D. E. Hein, H. J. Conlon, D. L. Hamilton, G. M. Mindrum, and L. Schiff. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **45**, 363–370, March, 1955. 10 refs.

At Cincinnati General Hospital (University of Cincinnati) the lipid content of 85 specimens of human liver obtained by needle biopsy for diagnostic purposes in a variety of cases was determined and compared with that of the serum. In 20 normal livers the total lipid content was found to range from 2·6 to 8·3 g. per 100 g. wet liver, with a mean value of 5·2 g. per 100 g. . In 5 of these 20 cases the serum lipid content was abnormally high, and in 4 of these 5 the lipid content of the liver was above the mean value for the group, but statistical analysis showed no significant association between the lipid content of the liver and the total lipid content of the serum or its content of any of the lipid fractions.

In 7 out of 11 cases of portal cirrhosis the liver lipid content was abnormally high, ranging from 9·6 to 27·0 g. per 100 g., but of 12 cases of other types of cirrhosis, only in 2 was the liver lipid content high. There was a significant but small positive association in these cases between the total lipid content of the liver and the serum levels of total lipids, fatty acids, phospholipids, and total and free cholesterol, but none between the liver lipid content and the neutral fat and esterified cholesterol contents of the serum. On average only 31% of the variations in liver lipid content from the mean value could be accounted for by variations in serum lipid content. The liver lipid content in a case of cirrhosis cannot therefore be predicted from the serum lipid content. In 12 cases of viral hepatitis the liver lipid content was within the normal range, and there was no significant association between the serum and liver lipid values. High liver lipid values were found in 5 out of 8 cases of fatty vacuolization, but there was again no significant association between the total lipid contents of serum and liver and the same was true of the 22 remaining cases, in which the diagnosis included focal necrosis, granuloma, metastatic carcinoma, and lymphoma.

H. Lehmann

917. **Abnormal Serum and Urine Proteins in Thirty-five Cases of Multiple Myeloma, as Studied by Filter Paper Electrophoresis**

E. F. Osserman and D. P. Lawlor. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 462–476, March, 1955. 10 figs., 44 refs.

The protein pattern in samples of serum and urine from 35 patients with multiple myeloma was examined at the Francis Delafield and Presbyterian Hospitals, New York, by the method of paper electrophoresis; a modified paper electrophoretic apparatus—which is claimed to give sharper resolution of protein fractions and greater uniformity and reproducibility of patterns—was used and is here described. The samples from all 35 cases showed characteristic protein abnormalities, homogeneous globulin peaks being demonstrated in both the serum and urine in 17 cases, in the serum only in 11 cases, and in the urine only in 7 cases. All urine samples giving a positive reaction for Bence Jones protein showed a characteristic electrophoretic abnormality, but in 8 of the 24 electrophoretically positive urine samples tests for Bence Jones protein were negative. Because of its relative simplicity, paper electrophoresis of urine is recommended as a practical clinical test in cases of myeloma.

Three cases, of which 2 exhibited unusual clinico-pathological features linking them with malignant lymphoma, and one well demonstrated the value of serial paper electrophoretic studies for appraising the efficacy of a therapeutic regimen for myeloma, are discussed in some detail. The physico-chemical properties of the proteins in the serum and urine of patients with myeloma and the possible nature of their interrelation are also considered. *J. E. Page*

MORBID ANATOMY AND CYTOLOGY

918. **Focal Paget's Disease of the Skull (Osteoporosis Circumscripta)**

D. H. Collins and J. M. Winn. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **69**, 1–9, 1955. 13 figs., 15 refs.

Since its original description as a radiological entity by Schüller (*Brit. J. Radiol.*, 1926, **31**, 156) osteoporosis circumscripta has been widely recognized as a form of focal rarefaction of the flat bones of the skull occurring in adults. In many instances the skull lesion appears to be an isolated one, but a number of cases have been recorded where indubitable lesions of Paget's disease of bone were present or were found to develop in other parts of the skeleton. The view is thus generally held that the condition is a manifestation of Paget's disease. A few pathological reports of isolated cases, including those of Sosman (*Radiology*, 1927, **9**, 396) and of Erdheim (*Beitr. path. Anat.*, 1935–6, **46**, 1), have de-

scribed histological changes similar to those seen in Paget's disease, but until now little pathological evidence regarding the nature of the condition has been available.

In the present paper are described 5 cases of osteoporosis circumscripta discovered in a careful survey of calvaria removed during necropsy at the General Infirmary at Leeds. This corresponds to an incidence of one in 350 to 400 necropsies; thus the condition is much less common than the usual form of Paget's disease. The ages of the 5 patients concerned—4 men and one woman—were respectively 43, 57, 61, 78, and 80 years. One case showed changes of Paget's disease in the bones of the pelvis.

In each of the 5 cases the histological characteristics of the skull lesions were those of Paget's disease of bone. Occasional thickened trabeculae showed the characteristic mosaic of cement lines separating areas of bone with disoriented lamellar structure, but the bulk of the abnormal tissue consisted of slender, newly formed bone trabeculae, conspicuous vascular spaces, and fibrous tissue. Bone resorption greatly exceeded new bone formation.

The authors accept the view that the initial lesion of Paget's disease is bone destruction. Because simple osteoporosis of senile type involved the vertebrae in 3 of the 5 cases they tentatively suggest that in osteoporosis circumscripta the failure of the productive phase that generally follows in Paget's disease may be associated with the same influences that impair osteoblastic activity in senile osteoporosis. *H. A. Sissons*

919. **Hürthle-cell Tumors of the Thyroid**
L. W. GARDNER. *Archives of Pathology* [*Arch. Path. (Chicago)*] **59**, 372–381, March, 1955. 14 figs., 35 refs.

A clinical and pathological survey of 46 cases of Hürthle-cell tumour of the thyroid gland seen at the Mount Carmel Mercy Hospital, Detroit, since 1940 is presented. The patients were 42 women and 4 men, a sex ratio of 10 to 1, and ranged in age from 16 to 72, the majority being between 25 and 50.

The tumours were usually solitary (38 cases), rounded, and encapsulated, and ranged in size from $1{\cdot}5\times1\times1$ cm, to $12\times10\times9$ cm., the average weight being 71 g. The cut surface was homogeneous and yellowish, with areas of haemorrhage or necrosis. Microscopically, the pattern was mainly trabecular in 23 cases, small alveolar in 12, large follicular in 6, and papillary in 5, but in about half the cases there was a mixture of these types. In 45 of the tumours there was no evidence of anaplasia or capsular invasion and definite mitotic figures were not observed. These cases, classified as Hürthle-cell adenomata, had been observed for between 2 and 22 years (in 28 cases (60%) for more than 8 years) after treatment by partial or subtotal thyroidectomy, and all the patients were alive and well. In the last case, however, following partial removal of a Hürthle-cell adenoma on two occasions 13 and 2 years previously, a further operation revealed the presence of carcinoma, with invasion of the capsule but not of the vessels. The patient died after operation, this being the only death in the series.

The literature is reviewed. Since in other reported series 30 to 100% of the tumours were classified as carcinomata, the author suggests that this was owing to the inclusion of tumours showing only some degree of Hürthle-cell change. He proposes that the term Hürthle-cell tumour should be strictly limited to those tumours composed wholly of cells with typical granular, eosinophilic cytoplasm. In these cases the prognosis is favourable. *M. C. Berenbaum*

920. **The Pathology of Paraplegia Occurring as a Delayed Sequela of Spinal Anaesthesia, with Special Reference to the Vascular Changes**
J. G. GREENFIELD, A. G. RICKARDS, and G. B. MANNING. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **69**, 95–107, 1955. 9 figs., 19 refs.

The authors describe the pathological findings in 3 cases in which the patient died with severe neurological disturbance 9 weeks to 6 months after undergoing an operation under spinal analgesia. The clinical signs and symptoms included paraplegia in all 3 cases, with ophthalmoplegia in 2 and optic atrophy and epileptic convulsions in one.

The main pathological changes consisted in extensive plastic pia-arachnoiditis with focal lacunary degeneration of white matter in the lower half of the spinal cord. Attention is drawn particularly to vascular changes in the meningeal arteries and veins of the lower thoracic and lumbo-sacral portions of the cord, consisting in collagenous replacement of the media, stretching and breakage of the elastica, and intimal proliferation without evidence of thrombosis. The pathogenesis of the lesions is discussed and it is suggested that they may be caused by the spinal analgesic itself or, more probably, a contaminant introduced with it. *L. Crome*

921. **The Influence of Chemotherapy and Antibiotic Treatment on the Morbid Anatomy of Tuberculosis in Man (with Reference to Personal Investigations).** (Pathologische Anatomie der Tuberkulose des Menschen nach chemotherapeutischer und antibiotischer Beeinflussung (unter Zugrundelegung eigener Untersuchungen))
G. HOLLE. *Zeitschrift für Tuberkulose* [*Z. Tuberk.*] **105**, 261–274, 1955. 21 figs., bibliography.

The introduction of chemotherapy into the treatment of tuberculosis has led to a new understanding of the metabolism of the tubercle bacillus and of its relation to the host. In particular, the theory that the tissue changes of tuberculous inflammation are largely allergic in nature has had to be drastically revised since it has been found possible to transform an exudative process into a productive one through inhibition of bacillary growth; thus the direct toxic effect of the bacillus on the tissues must be regarded as the main factor determining the tissue changes. The effect of chemotherapy on the morbid anatomy of tuberculosis, however, depends not only on the dosage given and the efficacy of the drug against the tubercle bacillus, but also on the possibility of its reaching the infective focus.

The present account of the morphology of tuberculous lesions under the influence of chemotherapy is based on

the examination, at the Pathological Institute of the University of Greifswald, of 30 cases of haematogenous tuberculosis (miliary tuberculosis and tuberculous meningitis) treated with streptomycin and 20 similar cases treated with thiosemicarbazone (thiacetazone) and partly with PAS. (In the latter group fewer necropsies were carried out than in the former, the findings being largely those of biopsy of the skin and of lymph nodes.)

Without chemotherapy the single tubercle heals either by fibrous organization or, if caseation is present, by encapsulation. Such encapsulation usually does not lead to complete restitution to normal of the tissues, in which lymphoid infiltration and giant cells persist; there is thus always a possibility of dissemination of infection through bacilli phagocytosed by the epithelioid cells present in such "healed" lesions. The histological picture of the healing of tuberculosis under chemotherapeutic influence is essentially different from that of spontaneous healing. Generally speaking, exudative processes become transformed into productive ones and specific reactions into non-specific. The single miliary tubercle, if entirely productive, undergoes a reticular fibrosis which may progress to complete healing. However, if caseation is present a fibrous capsule is developed, and although epithelioid cells are usually absent, complete healing is rare. Even with chemotherapy, therefore, complete regression of the lesions of haematogenous tuberculosis can be expected only in the absence of any considerable degree of caseation.

The morbid anatomy of tuberculous meningitis undergoes a still more extensive transformation under the influence of chemotherapy. Through fibrosis of the superficial layers of the leptomeninges and encapsulation of the deeper caseous exudate numerous solitary tubercles develop, and these play a much more important part in determining subsequent recurrences than the drug resistance of the organisms. After meningeal spread has ceased, the infection may be propagated through the ventricular system.

E. Forrai

922. **Pulmonary Vascular Changes in Coal-workers' Pneumoconiosis**

A. L. WELLS. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 573–587, 1954. 21 figs., 41 refs.

Changes in the pulmonary vessels of 388 South Wales coal-workers who had died with pneumoconiosis were studied at the Royal Infirmary, Cardiff. The cases were divisible into three groups: Group I, simple pneumoconiosis (181); Group II, massive pneumoconiosis (136); and Group III, pneumoconiosis and tuberculosis (71).

It was found that changes due to ageing were increased in some cases in Group I and in many cases in Groups II and III. (It had been shown in a previous post-mortem study of the same 388 cases (*Brit. Heart J.*, 1954, **16**, 74) that cor pulmonale was uncommon in Group I and specific changes due to dust were slight. In Groups II and III cor pulmonale was common and vascular changes due to pneumoconiosis were often severe.) There was old-standing thrombosis in arteries to diseased lobes, obstruction and obliteration of small arteries in the fibrotic parts, and reduction of capillaries by emphysema. Enlargement of bronchial arteries and of anastomotic shunts was demonstrated, but it was thought that any hypertension present was sufficiently explained by vascular obstruction. In the late stages, especially with circulatory failure, thrombosis of small vessels (both veins and arteries) was frequent. Other interesting observations were invasion of arteries by the anthracotic process and intimal ulceration, with medial thinning, of large arteries fixed to anthracotic foci.

D. M. Pryce

923. **Histological Changes in Sympathetic Ganglia in Essential Hypertension.** (Zur Frage histo-pathologischer Veränderungen an sympathischen Ganglien bei der essentiellen Hypertonie)

W. WALTER and F. MARCOS. *Deutsche Zeitschrift für Nervenheilkunde* [*Dtsch. Z. Nervenheilk.*] **172**, 482–494, 1955. 12 figs., 13 refs.

The authors have examined sympathetic ganglia removed at operation at the University Neurosurgical Clinic, Cologne, from 50 patients of the age of 20 or over suffering from essential hypertension and at necropsy from 12 control subjects. They found histological changes, consisting in ballooning of the ganglion cells, with large numbers of exhausted cells and "disturbance of the axon-harmony" (Stoehr) in all cases of hypertension. They do not assert, however, that the presence of such changes necessarily throws any light on the pathogenesis of the condition.

[The photomicrographs illustrating this article are of excellent quality.]

L. Michaelis

924. **Variations in Histochemical Findings in Liver Tissue Obtained by Biopsy**

A. BOGOCH, W. G. B. CASSELMAN, and H. L. BOCKUS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 273–279, March, 1955. 3 figs., 4 refs.

The authors report that in the examination of liver biopsy specimens from 2 patients under treatment at the Graduate Hospital, University of Pennsylvania, Philadelphia, marked variation was found in the distribution of lipids and glycogen in different parts of the same biopsy specimen. They therefore performed duplicate biopsies of the liver at operation in 3 further cases, specimens being taken at intervals of 3½ hours, 25 minutes, and 5 minutes respectively. In the first 2 cases slight variations in the amounts of glycogen and lipids were attributable to the surgical procedures carried out in the interval between the biopsies. However, in the third case, one of secondary biliary cirrhosis with slight multilobular cirrhosis, a marked difference was found in the amount of lipid demonstrated in the two specimens of liver tissue, although these were taken from adjacent, apparently similar, areas.

It is concluded that significant differences may occur in the amount of demonstrable lipid and glycogen in different parts of the same liver and even within the same biopsy specimen, and that this fact should be borne in mind in assessing histo-chemical findings in liver tissue.

M. C. Berenbaum

Microbiology and Parasitology

925. **Electron Microscope Studies of the Morphology of Pathogenic Spirochaetes**
R. H. A. SWAIN. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **69**, 117–128, 1955. 20 figs., 18 refs.

Working at Edinburgh University, the author has made a careful study, by means of electron micrographs of freshly fixed preparations, of the structure of the following species of spirochaete occurring in man: the Wijnberg strain of *Leptospira icterohaemorrhagiae*, a rabbit-adapted Nichols strain of *Treponema pallidum*, mouse-adapted strains of *Borrelia duttoni* and *Bor. recurrentis*, and an organism morphologically identical with *Bor. vincenti*. The spirochaetes were separated from cells and coarse particles by centrifugation, the supernatant fluid containing the organisms being then divided in 4 portions, one of which was fixed with 0·1% osmic acid immediately and the others after dilution with distilled water and standing for 2 hours, after treatment with trypsin for varying periods, and after treatment with pepsin for 10 minutes. The various portions were then purified and concentrated by differential centrifugation, the final deposits being suspended in distilled water and placed on a copper grid covered by collodion membrane. After shadow-casting with gold–palladium alloy the specimens were examined in an electron microscope using accelerating voltages of 75 and 100 kV.

True flagella were not found in any of the electron micrographs of freshly fixed preparations of these five species. Fibrils varying in number in different species were found in every case and seem to maintain the spiral shape of the organisms. The fibrils were often displaced when the cells were damaged by enzymatic digestion or changes in osmotic pressure. *L. icterohaemorrhagiae* was found to consist of a cylinder of homogeneous cytoplasm containing a single axial filament and bounded by a cell membrane. Electron micrographs of *T. pallidum* showed three fine fibrils wound spirally round the body of the organism almost certainly within the cell membrane. The latter was very resistant to trypsin, but was completely dissolved by pepsin within 20 minutes. During this process the fibrils might become distinct and sometimes protruded to give the appearance of bacterial flagella. *Bor. duttoni* had an outer covering of structureless, slimy material about 0·06 μ thick, which was readily digested by trypsin. Within this covering there were 7 to 12 fine fibrils, each about 0·02 μ in diameter, held together in the form of a band and wound round the body of the spirochaete external to the cell wall containing the cytoplasm. *Bor. recurrentis* had a similar structure, but the fibrils numbered 5 to 8 only and were twisted together to form a cord. *Bor. vincenti*, unlike the relapsing-fever spirochaete, had no external amorphous layer, but was enclosed by a definite cell membrane within which were 8 to 11 fibrils.

Encysted forms of *Bor. duttoni* and *L. icterohaemorrhagiae* were observed, especially in preparations that had been left to stand at room temperature. When stained with Giemsa's or Leishman's stain these cysts showed no sign of internal structure, but when examined with the electron microscope they were found to contain coiled-up spirochaetes. The cysts protruded from the spirals of apparently normal spirochaetes and ranged in diameter from 1·0 μ up to 3 μ, or even 4 μ in exceptional cases. Their structure suggested a resting phase rather than a stage of reproduction. *Edward Hindle*

926. **The Structure of Leptospirae as Revealed by Electron Microscopy**
J. W. CZEKALOWSKI and G. EAVES. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **69**, 129–132, 1955. 12 figs., 15 refs.

The authors have examined the structure of strains of *Leptospira icterohaemorrhagiae* and *L. canicola* with the electron microscope at the University of Leeds. The cultures were washed 4 or 5 times in distilled water and then suspended in aqueous solutions of sodium deoxycholate ranging in concentration from 0·01 to 1·0%. After exposure to this reagent for periods varying from 30 seconds to 30 minutes they were fixed in 5% osmic acid and drops of suspension allowed to dry on collodion-filmed grids and shadowed with chromium for examination with the electron microscope.

The organisms were shown to consist of two components—a cytoplasmic cylinder wound helically around a narrower and rigid axistyle. The latter is considered to lie for the most part outside the membrane enclosing the cytoplasmic cylinder, but in close contact with it, penetrating the cylinder just short of each end and terminating within it. [The difficulty of interpreting the results of electron microscopy is exemplified by the fact that Swain (see Abstract 925), using the same strain of *Leptospira*, came to the opposite opinion concerning the position of the axial filament in relation to the cell membrane.] *Edward Hindle*

927. **The Detection of Tubercle Bacilli in Sputum with Fluorescence Microscopy.** (La ricerca del bacillo di Koch nell'escreato con la microscopia a fluorescenza)
V. CALDERATO and G. PESCETTI. *Minerva medica* [*Minerva med.* (*Torino*)] **1**, 720–724, March 17, 1955. 3 figs., 19 refs.

The authors compared the efficacy of fluorescence microscopy with that of direct microscopical examination by the Ziehl–Nielsen method for the detection of tubercle bacilli in sputum. For the former method they used Herrmann's technique with slight modifications. They examined 5,499 sputa, in 664 of which a positive result was obtained with the fluorescence method and in 512 with the Ziehl–Nielsen method. In their opinion fluorescence microscopy is more reliable than direct microscopy, the tubercle bacilli being more easily distinguishable. *Franz Heimann*

928. **Studies on the Virulence of Tubercle Bacilli Resistant to Isoniazid.** (Études sur la virulence des bacilles tuberculeux résistants a l'isoniazide)
H. NOUFFLARD. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **88**, 325–335, March, 1955. 1 fig., 18 refs.

The author has endeavoured to confirm the statement that tubercle bacilli which have become resistant to isoniazid have lowered pathogenicity for laboratory animals. Of 4 strains of *Mycobacterium tuberculosis* isolated from patients treated with isoniazid and found to be resistant to the drug, 3 when injected into mice caused generalized infection which developed much less rapidly than infection with sensitive strains, and the organisms isolated from the lesions were resistant to isoniazid. Similar findings were noted with strains made resistant to isoniazid *in vitro*. On the other hand the fourth strain produced as severe an infection in mice as sensitive strains, and the organisms isolated from the lesions were found to be sensitive; it is suggested that this strain was heterogeneous. It was also found that resistant strains regained virulence on repeated animal passage, but their resistance to isoniazid was unaffected.

The author discusses the implications of these results for human tuberculous infections. He suggests that many patients treated with isoniazid may still be producing sputum containing resistant organisms. Although no infections of infants have been reported with strains of *Myco. tuberculosis* resistant to isoniazid on primary isolation, some of the resistant strains with lowered virulence may in fact be heterogeneous and contain more virulent organisms. There is also the danger that repeated cross-infection may enhance the virulence of a strain without reducing its resistance to the drug. The author concludes that it is probably wise to treat all tuberculous patients with a combination of drugs in order to reduce to a minimum the risk of producing resistant strains. *R. F. Jennison*

929. **The Length of Survival of Dysentery Bacilli in Dried Faeces.** (Длительность сохранения дизентерийных палочек в высохших испражнениях)
O. W. BYTCHKOVSKAYA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] No. 3, 19–22, March, 1955.

The survival in dried faeces of sulphonamide-sensitive and sulphonamide-resistant dysentery bacilli was investigated at the Institute of Epidemiology, Microbiology, and Hygiene, Sverdlovsk, the author having previously found that the resistance of the latter to a variety of influences was greater than that of the former.

To each gramme of a thick and even suspension of normal human faeces were added 20 million organisms of the dysentery strain to be investigated; 0·3 g. of this suspension was then spread evenly on disks 2·5 cm. in diameter made of cotton fabric, paper, wood, glass, or copper, dried, and then kept at temperatures of 37° C., 18° to 22° C., or 4° to 8° C. Immediately after drying and again at predetermined intervals the disks (except those of cotton fabric) were swabbed with cotton-wool swabs moistened in nutrient broth which were then washed for 5 minutes in test tubes containing 5 ml. of nutrient broth. The cotton-fabric disks were dealt with by cutting out small pieces and immersing them in 5 ml. of broth for 5 minutes. Two drops of the broth washings were then cultured on " endo " agar.

In general, *Shigella dysenteriae* (Shiga), *Sh. paradysenteriae* (*flexneri*), and *Sh. sonnei* survived longest at 4° to 8° C. and for comparatively short periods of 1 to 9 days only at 37° C. There was a marked difference between sulphonamide-sensitive and sulphonamide-resistant strains, the latter surviving 2 to 8 times longer than the former. Diffuse daylight had very little influence on survival, particularly with the strains of *Sh. flexneri* and *Sh. sonnei*. Differences in the composition of the faecal samples, even when these were obtained from the same person at different times, had a considerable influence on the length of survival, and only when the same sample of faeces had been used in all experiments could the results be compared. On the other hand, the material of which the disks were made had little influence on the length of survival, with the exception of copper which, as expected, had a marked oligodynamic action. Sulphonamide-resistant strains isolated as such from patients survived on the average twice as long (32 to 39 days at 4° C. and 11 to 30 days at 18° C.) as strains rendered resistant *in vitro*. *Sh. sonnei* tended to survive longer than either *Sh. dysenteriae* (Shiga) or *Sh. flexneri*. Its length of survival was equal to that of *Salmonella typhosa* and *Salm. paratyphi*.

The author suggests that the longer survival time of sulphonamide-resistant strains may be of epidemiological significance and may contribute to a wider spread of the infection. *K. Zinnemann*

930. **A New Technique for the Concentration of Microfilariae from the Venous Blood, and its Application to Their Detection in Persons Harbouring Them in Low Density; Together with Observations on the Significance of Such Low Densities**
R. M. GORDON and W. A. F. WEBBER. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **49**, 80–95, March, 1955. 4 figs., 24 refs.

From the Liverpool School of Tropical Medicine is described a technique for detecting (without accurate enumeration) scanty microfilariae in large volumes—for example, 10 ml.—of blood. The blood is haemolysed and then passed through a filter of stainless steel wire, which holds back the microfilariae. About 50 to 75% of the microfilariae present can be recovered and the morphology is well preserved. The technique was applied to samples of venous blood from 65 adult male Africans living in an area where loiasis is prevalent and compared with direct examination of a thick film of 50 c.mm. of blood obtained by finger-prick from the same subjects. Microfilariae were found by both methods in blood from 18 subjects, and a positive finding was made in 12 more samples by the new technique; in the other 35 cases both methods gave negative results. Although it is probable that all the Africans had been infected by *Loa loa* at some time, in only 46% of them were microfilariae shown to be present, even with this concentration technique. *F. Hawking*

Pharmacology

931. **Action of Histamine Liberator Compound 48/80 in the Guinea Pig. With a Review of Previous Reports of Its Action in Other Species**
S. M. FEINBERG and L. A. STERNBERGER. *Journal of Allergy* [*J. Allergy*] **26**, 170–179, March, 1955. 19 refs.

The toxicity of Compound 48/80, a condensation product of *p*-methoxyphenylethyl methylamine with formaldehyde and a potent liberator of histamine, was determined at Northwestern University Medical School, Chicago, in guinea-pigs after single injections and after repeated sub-lethal injections. When it was given as a 2% or 10% aerosol the animals showed irritation of the nose by scratching and some respiratory embarrassment, but not the symptoms typical of histamine or anaphylactic shock. The administration of "phenergan" (promethazine) did not protect against these symptoms, and necropsy on those animals which had succumbed to the injection of toxic amounts of the compound showed no emphysema, but a haemorrhagic, congested lung and a congested liver.

In a further study, when 8 guinea-pigs which had received 2 mg. of Compound 48/80 per kg. body weight daily for 6 days intraperitoneally were passively sensitized to egg albumen, they were found to be strongly protected against anaphylactic challenge with egg-albumen aerosol. Repeated daily injections failed to make the animals refractory to Compound 48/80. It is therefore concluded that the toxic effect of the compound is not caused by histamine release and depletion. These toxic effects, which are not yet fully understood, are an obstacle to the experimental use of the drug as a histamine liberator in the living animal. *H. Herxheimer*

932. **The Effect of Bentyl Hydrochloride on Intraluminal Pressures of the Stomach and Duodenum**
S. H. LORBER and H. SHAY. *Gastroenterology* [*Gastroenterology*] **28**, 274–280, Feb., 1955. 2 figs., 10 refs.

A method whereby continuous records of the pressure in the lumen of the stomach and duodenal cap are obtained by means of Levin tubes filled with saline and connected to strain gauges was used at Temple University School of Medicine, Philadelphia, to study the antispasmodic effect of the parenteral administration of "bentyl" (dicyclamine hydrochloride). The subjects were examined in the fasting state, the tube positions were checked by fluoroscopy, and a basal record made, which in normal subjects showed frequent small and occasional large waves.

To 26 subjects with "good" basal motor activity 5 to 40 mg. of bentyl was given subcutaneously or 5 to 200 mg. intramuscularly. The large-wave activity was depressed in some cases when 40 mg. was given subcutaneously, whereas 25 mg. given intramuscularly had the same effect and activity was usually abolished altogether by 50 mg. or more. On the average the effect began after 5 minutes and lasted one hour. When the drug was given in the same dosage to 15 patients with little or no basal activity, who first received 5 mg. of "urecholine" (β-methylcholine chloride urethane) subcutaneously, the depression of activity with each dose of bentyl was less, and responses were more variable.

To assess its clinical effect, bentyl was given by mouth to 16 patients with peptic ulcer, 15 with irritable colon, and 10 with ulcerative colitis. A dose of 12·5 to 50 mg. was needed thrice daily to obtain relief of symptoms, most patients requiring 25 mg., but the drug was ineffective in 8 cases. Dry mouth was a common complaint, and dizziness occurred twice with high dosage, but these side-effects were not troublesome.

The authors suggest that depression of large-wave activity may be sufficient for clinical effect, and that bentyl should be given in a dose of 25 or 37·5 mg. 3 times daily. *G. C. R. Morris*

933. **The Mode of Action of Antithyroid Drugs: Further Observations on *in vitro* Inhibition of Oxidative Protein Iodination**
R. FRASER, M. G. W. HANNO, and W. R. PITNEY. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **10**, 1–6, March, 1955. 2 figs., 17 refs.

The authors describe the use at the Postgraduate Medical School of London of two tests *in vitro*, the enzyme test and the peroxide test, in the investigation of the antithyroid activity of a number of drugs. For the enzyme test, which is the more reliable, milk enzyme powder is incubated with casein, xanthine, and radioactive iodide. The protein is then precipitated and the residual radioactivity in the supernatant determined; from this the degree of protein iodination which has occurred in the presence of the drug and in control tubes can be calculated. By this method (which is described in full) high activity was observed with carbimazole and methimazole, and moderate activity with thiouracil and iodothiouracil.

The peroxide test, in which 1 ml. of 0·1 M peroxide is substituted for the enzyme and the xanthine, measures the ability of a drug to interfere with non-enzymic protein iodination in a system containing peroxide, casein, and radioactive iodide. By this method resorcinol, sulphathiazole, and isoniazid were shown to possess antithyroid activity. In further studies with thiocyanate, L-thyroxine, *p*-aminosalicylate, and *n*-butyl-4-hydroxy-3:5-diiodobenzoate all these substances showed some activity in both tests, while perchlorate and quinine had no activity in either.

It is suggested that the results give an indication of the mode of action of antithyroid compounds, the more potent of them interfering with the iodination of protein by a peroxidase in the thyroid cells. The authors believe that the tests will prove useful for the preliminary

selection of drugs for their antithyroid activity, and also for the detection of such activity as an undesirable side-effect in drugs intended for prolonged administration for other purposes. *L. G. Goodwin*

934. **A Comparative Evaluation of the Hypnotic Potency of Chloral Hydrate and Trichloroethanol**
A. H. Owens, E. K. Marshall, G. O. Broun, C. G. Zubrod, and L. Lasagna. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **96**, 71–83, Feb., 1955. 6 refs.

A combined investigation was undertaken at three United States hospitals—Johns Hopkins Hospital, Baltimore, Firmin Desloge Hospital, St. Louis, and the Massachusetts General Hospital, Boston—to evaluate the hypnotic potency of chloral hydrate and trichloroethanol. Approximately 800 trials were carried out, the effect of each drug being compared with that of the other and with that of a placebo. In one set of tests the preparations were given in gelatin capsules and in another as a 1% (w/v) solution, the dose in all instances being 1 g.

The study indicated that both drugs were effective hypnotics. It had been hoped to show that trichloroethanol was superior to chloral hydrate, but only in one hospital was this found to be so, and then only when the drug was given in solution. *G. S. Crockett*

935. **Clinical Studies on Toxicity and on Hypnotic and Sedative Effects of Ro 1-6463, Noludar (3:3-Diethyl-2:4-dioxo-5-methylpiperidine)**
E. H. Loughlin, W. G. Mullin, J. Schwimmer, and M. Schwimmer. *International Record of Medicine* [*Int. Rec. Med.*] **168**, 52–60, Feb., 1955. 1 ref.

The effectiveness of "noludar" (Ro 1-6463; 3:3-diethyl-2:4-dioxo-5-methylpiperidine), a new compound with sedative-hypnotic properties and an analogue of "sedulon", was investigated at the Flower and Fifth Avenue Hospitals, New York. Pilot studies involving 40 patients indicated that the administration of 250-mg. doses of noludar at bedtime or 50-mg. doses three times a day during waking hours produced adequate nighttime and daytime sedation respectively without undesirable side-effects. A dose of 250 mg. of the drug was therefore administered to 100 patients, 57 of whom had difficulty in falling asleep, 31 complained of interrupted sleep, and 12 were unable to sleep because of pain. A good response (sleep being induced within 60 minutes and lasting over 6 hours) was obtained in 37 of the patients with "initial" insomnia, 20 of those with intermittent insomnia, and 4 of those whose insomnia was due to pain. Doses of 50 mg. of noludar given 3 times daily was found to provide an adequate degree of daytime sedation in 93 of 100 patients. In both groups medication was continued for 8 weeks.

No urinary or haematological abnormalities attributable to the drug were found in any of the 200 cases, and liver and kidney function tests performed in 10 cases showed no hepatic or renal damage. Of the 100 patients given the drug at night, 4 complained of morning drowsiness, 5 of drowsiness and vertigo, 3 of drowsiness and headache, 2 of vertigo, and one of headache. All these symptoms were mild and occurred during the first week of medication. Of the 100 patients treated by day, 13 complained of drowsiness and 3 of nervousness and excitement.

In a double-blind test with noludar, quinalbarbitone sodium, and placebo capsules carried out on 50 patients with severe "initial" insomnia it was found that the two hypnotics produced a significantly better soporific effect than the inert material. The difference between noludar and quinalbarbitone sodium as regards time taken to induce sleep was not statistically significant. The average duration of sleep induced by noludar was 5·9 hours and by quinalbarbitone sodium 6·5 hours, and it is pointed out that although this difference is statistically significant, from a clinical standpoint it is not important. *Robert Hodgkinson*

936. **Further Observations of Cardiovascular Effects of Pentaerythritol Tetranitrate in Animals and Man**
T. Winsor and C. C. Scott. *American Heart Journal* [*Amer. Heart J.*] **49**, 414–427, March, 1955. 5 figs., 15 refs.

An experimental and clinical study of the effects of pentaerythritol tetranitrate (PETN) on the circulation was carried out at the Hospital of the Good Samaritan, Los Angeles. In dogs sublingual administration of 40 mg. PETN resulted in an increase in coronary flow averaging 11·5%, a slight fall in blood pressure being taken as indicating coronary vasodilatation. In patients with coronary insufficiency and angina pectoris there was very little alteration in pulse rate, blood pressure, or peripheral circulation after 20 mg. of PETN given sublingually. The force of cardiac contraction after this dose, as recorded ballistocardiographically, showed an increase which, though slight, was regarded as significant.

In 12 patients suffering from angina of effort the administration of 25 mg. of PETN sublingually resulted in improvement in their exercise tolerance as measured on a treadmill. Acute attacks of angina of effort in 20 patients were treated by sublingual administration of 10 or 20 mg. of PETN and the results compared with those of nitroglycerin and placebos. That nitroglycerin proved more effective than PETN was attributed to the slower onset of action of the latter. Four patients obtained some relief in acute attacks of angina of effort by inhalation of 19 mg. of powdered PETN. Long-term studies of the effect of PETN on nitroglycerin requirements were made on 13 patients, who were given for consecutive three-month periods (1) inert tablets, (2) large doses of PETN (70 mg. daily), and (3) small doses of PETN (35 mg. daily). It was found that the amount of nitroglycerin required by these patients was markedly reduced during PETN therapy, especially when larger doses were used.

The relatively rapid action of PETN after sublingual administration compared with its slow action after the swallowing of whole tablets proved clinically of most value in delaying and attenuating attacks of angina and in preventing anginal attacks when taken 20 minutes before exercise. *Bernard Isaacs*

Chemotherapy

937. **Post-operative Staphylococcal Enterocolitis during Antibiotic Therapy**
B. J. FOWLER. *British Medical Journal* [*Brit. med. J.*] **1**, 1313–1315, May 28, 1955. 26 refs.

Staphylococcal enteritis occurring during antibiotic therapy is now of clinical importance, and a number of cases have been reported in the literature. In this paper 3 further cases, all of which were fatal, are described. Each patient had had an abdominal operation and been given a combination of antibiotics. Although only small doses of these drugs had been used, vomiting, diarrhoea, and collapse occurred between the 3rd and 6th days of the treatment. Response to intravenous fluid therapy and to other antibiotics was very poor. At necropsy pathogenic staphylococci resistant to the antibiotic given were grown from the yellow, watery intestinal contents. The gut was acutely inflamed in only one case.

It is suggested that the routine prophylactic administration of antibiotics is inadvisable in abdominal surgery. However, should infection ensue after such routine use, early diagnosis of the condition is essential; this may be made from the clinical state and confirmed by the demonstration of Gram-positive cocci in the faeces.

E. G. Rees

938. **The Action of Nystatin (Fungistatin) *in vitro* and *in vivo* on *Candida albicans* and other Yeast-like Fungi.**
(Action de la nystatine (fungicidine) *in vitro* et *in vivo* sur *Candida albicans* et autres champignons levuriformes)
E. DROUHET. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **88**, 298–314, March, 1955. 2 figs., 22 refs.

Working at the Pasteur Institute, Paris, the author has studied the effect of the antibiotic "nystatin" (fungistatin) on strains of *Candida* and *Geotrichum*. Tests *in vitro* on 55 strains of *Candida* and 5 strains of *Geotrichum* showed that the concentration of the antibiotic inhibiting growth of the organisms varied between 1·56 and 12·5 μg. per ml.; it was 2 or 3 times more effective in liquid culture media than on solid media, and its action was fungicidal as well as fungistatic.

In the tests carried out *in vivo* on rabbits infected with *C. albicans* by way of the digestive tract nystatin caused a considerable reduction in the numbers of organisms excreted. Whereas usually the mortality of rabbits infected intravenously with *C. albicans* is 100%, the intravenous injection of 40 mg. of nystatin per day for 5 days reduced the mortality to 62·5%. When given to rabbits by mouth the antibiotic caused no toxic effects even in doses up to 3 g. per kg. body weight.

Clinically, 35 cases of generalized and localized infection with *C. albicans* in children were treated with marked clinical and bacteriological improvement. The administration of 0·2 and 1 g. of nystatin daily by mouth for 4 to 5 days resulted in the disappearance of the organisms from the mouth, faeces, urine, and blood within 5 days. Of these cases, 3 relapsed about 2 weeks after the cessation of treatment.

R. F. Jennison

939. **Antituberculous Effects of Certain Surface-active Polyoxyethylene Ethers**
J. W. CORNFORTH, P. D'ARCY HART, G. A. NICHOLLS, R. J. W. REES, and J. A. STOCK. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **10**, 73–86, March, 1955. 9 figs., 22 refs.

In studies carried out at the National Institute for Medical Research, London, the authors have shown that tuberculosis produced experimentally in mice and guinea-pigs can be suppressed by treatment with the non-ionic surface-active agent "triton A20". This mixture of polymers is prepared by condensing octylphenol with formaldehyde, heating the product, and allowing the resulting resin to react with ethylene oxide to form a water-soluble syrup. The authors have now prepared eight series of polyoxyethylene ethers from tertiary butyl- and octylphenol with different degrees of molecular size, some being linear and others macrocyclic in structure. [Reference must be made to the original paper for the details of preparation and the chemical characteristics of these compounds.]

When tested upon mice infected with tuberculosis some members of the series showed activity comparable with that of streptomycin. It was demonstrated that this antituberculous activity was a property of the polymers, and not of some unknown contaminant. Ethers derived from small linear polymers containing less than 3 phenolic nuclei were inactive and caused haemolysis both *in vitro* and *in vivo*, but the toxic properties were decreased and the activity increased by increasing the molecular size. Maximum activity was shown by polymers having chains of ethylene oxide of an average length of 15 to 20 units; compounds with chains of greater length were inactive, while those with chains of over 45 units acted as "protuberculous" substances, producing a stimulant effect on the tuberculous process in the mouse. These changes from an inhibitory to a stimulant effect were associated with a decrease in the lipophilic:hydrophilic ratio. None of the active compounds or blood or tissue fluids from animals treated with them had any action upon the tubercle bacillus *in vitro*. Some of the compounds caused lipaemia and depletion of lipids in the adrenal cortex, but neither this effect nor the degree of ability to produce dispersed growth of tubercle bacilli *in vitro* was related to chemotherapeutic activity. The authors suggest that the substances act primarily through the host's defence mechanisms against tuberculous infection. It was shown that active compounds enter monocytes *in vivo* and appear to enhance their ability to suppress the intracellular multiplication of tubercle bacilli.

L. G. Goodwin

Infectious Diseases

940. **Decompression Treatment of Whooping-cough. A Clinical Survey of 903 Cases**
H. S. BANKS. *British Medical Journal* [*Brit. med. J.*] 1, 1052–1055, April 30, 1955. 9 refs.

From Park Fever Hospital, Lewisham, London, comes this report of the treatment of 903 children with whooping-cough by exposure to low atmospheric pressure in a decompression chamber. The procedure consisted in a simulated " ascent ", taking about 20 minutes, to a pressure equivalent to a height of 12,000 feet (3,600 m.); this was maintained for 45 minutes and was followed by a " descent " over 25 minutes. In 24 cases the treatment was repeated. The importance of selecting only suitable cases is stressed; in this series patients were selected for treatment if they had been coughing for 3 weeks, were not too ill or cyanosed, and if the pulmonary radiological changes were not gross. (It was not found possible to arrange a control group, and the disadvantages resulting from this are discussed.)

The study extended over 5½ years and the assessment of results in respect of 782 of the cases for which adequate information was available was largely based on the combined impressions of the patients' parents and the physicians. Cough and vomit records were kept by parents or nursing staff for 48-hour periods just before and again one week after treatment [but the details are not given.] The records showed that 28·2% of the patients underwent marked improvement after 4 to 7 days and a further 34·1% showed more gradual improvement. Vomiting stopped in 57·7% of the children with this symptom a few days after treatment, and in 20% it was greatly reduced. The mode of action of decompression treatment is not known, but a plea is made by the author for adequately controlled investigation, preferably including biochemical studies; this is particularly necessary in a disease like whooping-cough which has so far resisted all " successful " treatments.

David Morris

941. **Pertussis and Antibiotics.** (Pertussis och antibiotica)
U. CLAESSON and B. LINDQUIST. *Nordisk Medicin* [*Nord. Med.*] 53, 799–801, May 19, 1955. 4 figs., 11 refs.

942. **Migraine as a Sequel to Infection by *L. icterohaemorrhagiae***
J. B. ATKINS. *British Medical Journal* [*Brit. med. J.*] 1, 1011–1012, April 23, 1955. 9 refs.

In a study of the health of men working in the South Wales coalfield special attention was paid to the after-effects of Weil's disease (leptospiral jaundice). Migraine was found to be a common sequel to the disease, being recorded in 24 out of 50 such cases. Its incidence was evenly distributed among the various age-groups and among the men from various areas of the coalfield. In a control series of 50 men known to be serologically negative for *Leptospira icterohaemorrhagiae* the incidence of migraine was 12% (6 cases), a figure considerably higher than that reported in the literature for series comprising both men and women. The diagnosis of migraine was made if recurrent headache was associated with a gastro-intestinal disturbance or with visual symptoms, especially scintillating scotomata.

As judged by the finding of a mean resting diastolic blood pressure of more than 100 mm. Hg, a diagnosis of hypertension was made in 6 cases, 8 men suffered from attacks of giddiness, and 6 complained of numbness, tingling, and clumsiness of the hands. The author suggests that these findings may be of significance in relation to the concept of migraine as a localized cerebral vasomotor disorder allied to Ménière's syndrome. He also points out that it may be possible to link the incidence of migraine with the fact that meningitis is often a feature of Weil's disease. This linkage, if established, would account for the occurrence of vasomotor disturbances in the present cases. At all events, in areas in which infection with *L. icterohaemorrhagiae* is prevalent it would seem advisable to carry out agglutination tests in the preliminary investigation of any case of migraine.

A. Garland

VIRUS INFECTIONS

943. **ACTH in the Treatment of Infectious Hepatitis**
E. C. JOHNSON and H. D. BENNETT. *Gastroenterology* [*Gastroenterology*] 28, 265–273, Feb., 1955. 1 fig., 8 refs.

In the course of one year all patients admitted to the Veterans Administration Hospital, Hines, Illinois, with acute infective or serum hepatitis, totalling 22, were treated with ACTH, and the results are here compared with those obtained in 32 cases during the previous year, when the treatment given was basically similar, but ACTH was not given. All patients were kept in bed and given a generous diet with extra vitamins and choline, being allowed up only when the results of liver function tests were normal. ACTH was given intravenously, 10 mg. in 1,000 ml. of 5% glucose solution twice daily for the first 3 days and once daily thereafter. The two groups were comparable initially in their response to tests of liver function, and the illness had been present for an average of 15 and 17 days in the treated and control groups respectively.

The average duration of symptoms after admission was 13 days in the treated group and 10·4 days in the control group. The results were also judged in terms of the average time taken for the return to normal of the results of liver function tests. This was less in the treated group for the thymol turbidity and cephalin flocculation tests, less in the control group for the serum

bilirubin level and prothrombin time, and equal for all other tests. [The significance of the differences is not expressed statistically.] Liver biopsy, performed in a few cases, showed the usual picture of the disease in both groups. The results of one or more liver function tests were still abnormal in two-fifths of each group at the end of the period of observation, which lasted an average of 7 months in the treated and 6 months in the control group. The serious complications encountered in the treated group included perforation of a peptic ulcer in one patient, an exacerbation of diabetes in another, and recrudescence of healed osteomyelitis in a third; cases of lung infection, euphoria, and reactive depression also occurred. Three case reports are included.

The authors conclude that the danger of complications of ACTH treatment outweighs any advantage to be gained from its apparent immediate good effect in acute hepatitis, and that it has no detectable long-term effect; but they suggest that " an occasional extremely ill patient might be tided over during a critical period by the judicious use of ACTH therapy ".

G. C. R. Morris

944. **Clinical Pathology of Yellow Fever**

N. W. Elton, A. Romero, and A. Trejos. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 135–146, Feb., 1955. 3 figs., 20 refs.

The clinical and clinical pathological findings in 157 cases of yellow fever studied during the recent outbreak in Costa Rica (1951–3) are presented, and the morbid antomy of the disease, as seen in 11 fatal cases occurring in Panama and the Canal Zone between 1948 and 1952 are described. The hepatic lesion in these last cases consisted in an extensive acidophilic necrosis of the cytoplasm of the polygonal cells. Distribution was not always mid-zonal and there was no selective central necrosis, but the cells at the periphery of the lobule were commonly the least involved. Inflammatory changes and bile retention were minimal or absent. Intranuclear inclusion bodies were not observed. The intensity of the liver lesion was greatest about the 5th or 6th day, after which renal failure was predominant as the cause of death. The renal lesion was essentially similar to that of " lower nephron nephrosis ". There were no specific lesions in other organs, but haemorrhage from the mucosa was common in the stomach and upper gastro-intestinal tract. The cerebrospinal fluid not infrequently contained bile pigments.

The clinical pathology, as seen in the Costa Rican cases, is discussed in detail. In fatal cases an increase both in the total serum bilirubin level and in the " one-minute direct " value was demonstrable as early as the 3rd day. A sharp increase in jaundice (largely due to one-minute direct bilirubin) occurred on the 4th and 5th days, reaching on the 6th day a maximum which was maintained for some time. In non-fatal cases the serum bilirubin values were normal on the 3rd day and clinical jaundice did not develop until the 6th day, diminishing rapidly after the 7th day. In a few cases the jaundice developed later and reached a maximum in convalescence, regressing slowly thereafter (up to 30 days). It is concluded that the development and course of the jaundice can be used as a guide to the prognosis of individual cases. On the 3rd day the serum cholesterol level averaged about 140 mg. per 100 ml. in fatal cases and 169 mg. per 100 ml. in non-fatal cases. A decline to values below normal occurred in the critical phase in both groups, while high normal values developed on recovery. The total plasma protein content fell in all cases, especially in fatal ones, and rose rapidly during convalescence. The results of standard flocculation tests were mainly negative in the 1st week, becoming positive in both groups in the 2nd week.

Determination of coagulation and bleeding times and platelet counts gave no useful information, but the prothrombin time as determined by Quick's method was useful in prognosis, as values below 25% of normal between the 4th and 9th days of the illness were, with one exception, encountered only in fatal cases. The blood urea content rose progressively in fatal cases up to the 7th day and remained high thereafter until death, whereas in non-fatal cases there was a smaller progressive rise up to the 5th day, followed by a steady decline. Eosinopenia was a constant feature of the peripheral blood picture and was sustained in all severe cases, a rise in the eosinophil count being a favourable prognostic sign.

Clinically, the onset of the disease was sudden, with chills in most cases. Headache and backache were very common. The vomit was bile-stained in the first 3 days in about half the cases and blood-stained in one-fifth, being at first red and later black or chocolate coloured. Only in 2 of the fatal cases did the patient not vomit blood. Oliguria was observed in 30 cases, and anuria in 18 of 43 fatal cases. A slow, full pulse, with pronounced dissociation of pulse and temperature, was noted in 109 cases. The pulse rate did not fall below 60 beats per minute. Death occurred most commonly between the 6th and 8th days.

The authors emphasize in conclusion that the primary lesion of yellow fever is hepatitis, the most serious secondary disturbance being the appearance of lower nephron nephrosis.

B. G. Maegraith

945. **Roseola Infantum: 13 Cases Seen in General Practice**

E. L. McQuitty. *British Medical Journal* [*Brit. med. J.*] **1**, 1005–1006, April 23, 1955. 10 refs.

Roseola infantum, also called exanthem subitum, is a common (though little-known) disease which occurs in all parts of the world. It usually attacks infants between the ages of 6 months and 2 years, but may occur at even younger ages, while adults may be affected. The disease is ushered in with pyrexia accompanied by symptoms of inflammation and congestion of the nose and throat and frequently of the tympanic membranes. All symptoms subside rapidly on the appearance of the rash, which consists of discrete, rose-coloured macules most marked on the trunk, though when the rash is severe some coalescence may occur. The cervical and occipital lymph nodes are enlarged and there is a well-marked neutropenia during the febrile stage. Complications are un-

usual, though severe cases of suppurative otitis media and rhinitis following the illness have been reported. Death is rare. Treatment of the condition in uncomplicated cases is purely symptomatic.

The author discusses the differential diagnosis and gives details of 13 cases seen in his own practice. He makes a plea for the more frequent diagnosis of this condition, pointing out that in the past it has been obscured by the tendency to dismiss rashes in infants as due to more obvious causes, such as teething or drug sensitivity. *Winston Turner*

946. **The Neurological Manifestations of Cat Scratch Disease**
L. WEINSTEIN and R. H. MEADE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 500–505, May, 1955. 14 refs.

SARCOIDOSIS

947. **The Involvement of the Muscles in Boeck's Sarcoidosis.** (La participation de la musculature à la maladie de Besnier-Boeck-Schaumann)
P. A. MAURICE. *Helvetica medica acta* [*Helv. med. Acta*] **22**, 16–42, Feb., 1955. 6 figs., bibliography.

There has been some confusion between the myositis of Boeck's sarcoidosis and that due to muscular involvement in tuberculosis. The author gives a histological and clinical description of Boeck's sarcoid and suggests that many cases described as tuberculous myositis may in fact have been sarcoidal. In order to determine the frequency of muscular involvement in Boeck's sarcoid and whether muscle biopsy could confirm the clinical diagnosis, the author has examined, at the Institute of Pathology, Geneva, muscle tissue from 13 cases of confirmed or suspected sarcoid, the material being obtained in 6 cases at necropsy, in one after amputation of the legs, and in 6 by muscle biopsy. Detailed accounts of most of these cases are given, with illustrative photomicrographs.

Of the 6 cases examined post mortem, sarcoidosis was confirmed histologically in 5, although clinically the diagnosis had been made in only 2. The histological diagnosis was made on the finding of non-caseous lymphoepitheloid nodules, these often containing multinucleated cells. The case examined after amputation may have been one of sarcoidosis, despite the finding of a positive Mantoux test and evidence of pulmonary calcification. Of the muscle biopsy specimens, 5 were from definite cases of sarcoidosis and one doubtful; of these, 3, including the doubtful case, were confirmed histologically. One case exhibited localized muscular atrophy, but in the others clinical signs gave no clue as to a suitable site for biopsy and therefore under local analgesia specimens were taken from the biceps, deltoid, and quadriceps muscles. Biopsy examination before and after treatment with cortisone and ACTH in one case showed disappearance of epithelioid cells but persistence of fibrosis. In only one patient was tuberculous polymyositis observed.

The author concludes that tuberculous myositis is very rare. He points out that muscle biopsy is of value in differentiating sarcoidosis from the "collagenoses" such as rheumatoid arthritis, scleroderma, periarteritis nodosa, and disseminated lupus erythematosus. The histology of these diseases is briefly discussed. *D. Goldman*

948. **The Kveim Test in Sarcoidosis**
D. G. JAMES and A. D. THOMSON. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 49–59, Jan., 1955. 8 figs., 17 refs.

Kveim antigen consists of a 1-in-10 saline suspension of sarcoid lymph node, sterilized by heating at 56° C. for 2 hours on 2 successive days, diluted with saline to a final concentration of 1 in 20, and preserved with 0·25% phenol. In an investigation of its specificity at the Middlesex Hospital, London, the Kveim test was performed on 16 patients with sarcoidosis, 28 with tuberculosis, and 19 with other diseases, 0·2 ml. of the antigen being injected intradermally into the flexor aspect of the forearm.

A positive reaction to the Kveim test is the appearance at the site of injection after a few days of a small dusky-red papule, which develops to a palpable nodule by the end of a month, and persists, with or without further development, for several months. This papule is about 5 mm. in diameter, but may be larger. Of the 16 patients with sarcoidosis, 12 gave such a reaction. This was similar in appearance in all cases and consisted of one or more cellular foci in the dermis. The histological picture was that of sarcoid, and the lesions, about 2 to 5 mm. in diameter, consisted of avascular masses of epithelioid cells with varying degrees of fusion and degeneration of their nuclei. Necrosis was trifling and did not affect the reticulin fibres; giant cells, mainly of Langhans type, were present, and the whole was surrounded by a zone of lymphocytes and histiocytes, with a few plasma cells and occasional eosinophil granulocytes. In the remaining 4 cases there was no visible or palpable reaction.

In 3 of the 28 cases of tuberculosis a knot of tissue about 3 mm. in diameter was just palpable under the skin, but in none of the cases did a dusky-red papule develop. The histological picture in these 3 cases was similar to that in patients with sarcoidosis, but the necrosis was far more extensive, involving the collagen outside the cellular area, and the reticulin was destroyed in the necrotic area.

A foreign-body giant-cell reaction was noted in 3 of the 19 control cases and a non-specific cellular reaction in a further 6, the latter consisting in a focal lymphocytic reaction without necrosis in the superficial dermis. No other reaction was observed in the control group.

The authors conclude that the Kveim test is of considerable value as a diagnostic procedure in sarcoidosis and that, as the nodule produced by the test appears to show changes similar to those occurring in the spontaneous lesions in the same patient, it provides a means of assessing the activity and progress of the disease and of evaluating the results of various methods of treatment. *C. L. Oakley*

Tuberculosis

949. **Primary Tuberculosis in the Adolescent and the Adult.** (L'infezione tubercolare primaria nell'adolescente e nell'adulto)
G. Pescetti, U. Demichelis, and G. Randone. *Minerva medica* [*Minerva med.* (*Torino*)] **1**, 699–710, March 17, 1955. 11 figs., 34 refs.

Primary tuberculosis appears to occur more frequently among young adults than was hitherto believed to be the case. Of 500 patients between the ages of 15 and 35 suffering from pulmonary tuberculosis, 77 (49 males and 28 females) were considered to have a primary lesion. Of these, 88·7% were betweed the ages of 15 and 24.

From a study of these cases the authors conclude that the prognosis of primary infections in this age group is fairly good, although regression of the lesions is slower and less complete than in childhood, cavitation is more common, and complications due to rupture of a caseous lymph node into the bronchus more frequent.

Franz Heimann

DIAGNOSIS AND PROPHYLAXIS

950. **Tuberculin Sensitivity and Tuberculosis in 1,779 Nurses**
G. Poole. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **48**, 230–237, July, 1954 [received Feb., 1955]. 1 fig., 13 refs.

Since 1939 all student nurses on entering the preliminary training school of the Queen Elizabeth Hospital, Birmingham (a general hospital to which a certain number of tuberculous cases are admitted) have been subjected to a Mantoux test and radiological examination. Subsequently radiographs are taken three-monthly. Mantoux-negative entrants are re-tested during their training, and since 1950 B.C.G. vaccination has been offered to them. In this paper the records of 1,779 nurses entering the hospital between 1939 and 1952 are analysed and comparisons made with other surveys, notably the Prophit Survey (*Lancet*, 1944, **2**, 165).

Throughout the whole period 0·1 mg. of old tuberculin was used, though other strengths were also employed after 1949. At age 18, 57% of the entrants were Mantoux-positive, while at age 25 and over the figure rose to 78·5%. (The Prophit Survey figures were 80·6% at age 18 and 86·7% at age 24 and over.) In the period 1939–40, of some 200 girls who started training, over 70% gave a positive reaction; in 1951–2, when there were 300 entrants, the incidence was 50·5%. These percentages, which are total figures and include all age groups, are in agreement with those of the Prophit Survey. The Mantoux conversion rate was 72·9% (229 of 314 nurses negative on entry and whose records were complete), conversion taking place at an average of 13·5 months from the start of training. Erythema nodosum occurred in 10 nurses. The longest time between conversion and the development of erythema nodosum was 9 months; in one case the first positive Mantoux reaction was recorded at the onset of the disease. In 8 cases the condition was thought to have occurred as the hypersensitive manifestation of a disease other than tuberculosis; 3 of these cases were recorded in nurses who were Mantoux-positive at the time of entry. Tuberculosis developed in 40 nurses, 25 of whom were initially Mantoux-negative. One nurse died of tuberculous meningitis; the other 39 all had pulmonary or pleural disease. The proportion of initial positive reactors was the same whether the nurses had had a previous occupation or not, but it was greater in the group of girls (126) who had had 2 years' experience of nursing before entering the Queen Elizabeth Hospital.

The danger in the 12 to 18 months after Mantoux conversion is stressed, for it is during this critical period that conditions due to hypersensitivity may develop, and if tuberculosis is to follow conversion, it will probably appear during this time. *Thomas Marmion*

951. **Tuberculin-testing of a School Population (Musselburgh, 1953)**
W. A. Murray, P. W. R. Petrie, and J. Williamson. *British Medical Journal* [*Brit. med. J.*] **1**, 1178–1182, May 14, 1955. 4 figs., 6 refs.

In the Scottish burgh of Musselburgh, which lies near Edinburgh and has, with its surrounding area, a total population of about 21,800, the authors carried out tuberculin-testing of nearly the whole school population, followed by mass radiography of the positive reactors and clinical and radiological examination of the contacts of this group. The first skin test employed was the tuberculin jelly test, modified by the flour-paper technique, and the second test was a Mantoux 1 in 100 (100 tuberculin units) on all the negative reactors. The criteria for a positive reaction were 6 or more papules or an induration area 5 mm. or more in diameter at the site of inoculation and no reaction at the control site. In all, 3,282 school-children (93·5%) were tested, of whom 101 had previously been vaccinated with B.C.G. and were tuberculin-positive as a result; these cases were excluded from the subsequent analyses.

There was no difference in the incidence of positive reactors between boys and girls; 1,128 of the children were judged to be tuberculin-positive (excluding those who had B.C.G. vaccination earlier), representing a tuberculin-positive rate of 35·3%. Of the children aged 5 and 6 years, 26·3% were tuberculin-positive, and this figure rose to 50·0% in those aged 15 years; this rise was not gradual, but occurred in jumps at ages 9 and 12, corresponding roughly to the infant, primary, and secondary scholastic grouping. Of the 1,128 positive

reactors, 95·8% were examined radiologically by a mobile mass radiography unit which visited the schools. Among these, 6 children were subsequently notified as having active pulmonary tuberculosis and 3 others remained under observation because of minimal radiological abnormalities. Among the home contacts of children with positive reactions, 5 were found to have "abnormalities warranting notification" and 6 others were placed under observation, while among other adults coming voluntarily for examination there were 5 further notifiable cases, and 6 more were put under observation. Thus 10 adult cases of tuberculosis were discovered, giving a rate of 2·5 per 1,000 examined.

The results of this survey showed a high number of positive reactors at all ages as compared with the investigation carried out in England and Wales under the auspices of the Medical Research Council (*Lancet*, 1952, 1, 775; *Abstracts of World Medicine*, 1952, **12**, 183). In the rural parts of the district around Musselburgh the incidence of positive tuberculin reactors was much lower than in the urban areas, presumably mainly because of the better housing conditions. The authors conclude that this method of tuberculin survey was shown to be inefficient as a case-finding method for active tuberculosis, both among children and also among their contacts. At the time of this survey an equal number of cases came to light through mass radiographic examination of the general public.

[The validity of these observations depends on the view taken of the validity of the tuberculin tests employed, about which there is considerable doubt. Both the flour-paper variant of the tuberculin jelly test and that with 100 tuberculin units (Mantoux 1 in 100) can and do frequently give rise to false positive reactions, whatever the technique of examination. It is possible, therefore, that the actual number of infected children was much less than that suggested by the survey. This may explain the small proportion who were found to have active tuberculous lesions on radiological examination and the small number of contacts found to have active tuberculosis.] *John Lorber*

952. **Clinical Study of a Test for Immunity to Tuberculosis.** (Étude clinique d'un test d'immunité tuberculeuse)

D. MICHETTI and J. FELBER. *Schweizerische Zeitschrift für Tuberkulose* [*Schweiz. Z. Tuberk.*] **12**, 41–64, 1955. 29 refs.

On the assumption that the severity of a tuberculous infection is directly related to the virulence of the bacilli and inversely to the resistance of the host organism the authors have studied the reaction of sanatorium patients to B.C.G. injected intradermally and attempted to draw conclusions about the state of immunity to tuberculosis and the clinical development of the disease. For this purpose they injected intradermally 0·1 ml. of fresh Danish B.C.G. suspension (0·75 mg. per ml.) and noted the size of the resulting papule and the time taken for development of central ulceration in 326 tests on 239 patients, the results being compared with the clinical findings and course of the disease.

Although the number of cases studied is not yet sufficient for firm conclusions to be drawn, they are of the opinion that with further experience the test should prove helpful in the therapeutic, prognostic, and prophylactic fields. *Franz Heimann*

BONE AND JOINT TUBERCULOSIS

953. **Experimental Studies on the Treatment of Bone and Joint Tuberculosis with Dihydrostreptomycin and *iso*-Nicotinic Acid Hydrazide**

F. BASTOS MORA and L. PORTAL LLAMEDO. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **37A**, 156–168, Jan., 1955. 12 figs., 6 refs.

In a study carried out at the University of Barcelona the authors observed the effects of treatment with dihydrostreptomycin and isoniazid on experimentally induced tuberculosis of the bones and joints of rabbits and guinea-pigs. An emulsion of a strain of bovine tubercle bacilli (Vallée) of proved sensitivity to dihydrostreptomycin was prepared from a potato subculture, and 0·05 ml. of this emulsion was injected by special trocar into the marrow of the lower end of the femur of 20 rabbits, of which 10 served as untreated controls; the remaining 10 received 0·05 g. of dihydrostreptomycin intramuscularly twice daily for 6 weeks, treatment being started 45 days after inoculation. Bone lesions developed in only 4 of the experimental and in 3 of the control group. In the untreated animals these took the form of caseous foci filling almost the whole marrow cavity, surrounded by a large area of ill-demarcated lymphocytic infiltration. In the treated group the foci were much smaller, showed no softening, and were clearly demarcated from the surrounding healthy marrow by a narrow zone of lymphocytes.

In a second study the injection of 0·05 to 0·1 ml. of the same emulsion into the pre-patellar synovial fold of rabbits or guinea-pigs produced in the untreated animals an arthritis comparable to that seen in man; the lesions ranged in extent from a caseous synovitis (after 6 weeks) to destruction of the articular surfaces and underlying bone in the later stages. The guinea-pigs developed, in addition, lymphadenitis. Ten rabbits were treated for 50 days after inoculation, 5 with twice-daily injections of 0·05 g. of dihydrostreptomycin and 5 with 3 μg. of isoniazid given orally twice daily; limited gross lesions were observed in the joint of 3 of the animals, but the remaining 7 all showed microscopic evidence of tuberculous infection of the joint. In another group in which treatment was started 45 days after inoculation there was no difference between 10 controls and 20 treated rabbits, caseous infiltration of the entire joint being noted in all the animals.

In a similar experiment with 40 guinea-pigs the controls showed caseation and infiltration of the synovial membrane and moderate lymphadenitis after 35 days; there was extensive involvement of the whole joint, with extracapsular abscesses, and marked inguinal adenitis developed after 3 months. Treatment with 0·04 g. of dihydrostreptomycin daily or 6 μg. of isoniazid for 50

days, starting 35 days after inoculation, led to only microscopic lymphatic involvement and slight swelling of the joint, with in many cases only microscopically demonstrable infiltration of the synovial membrane.

H. F. Reichenfeld

RESPIRATORY TUBERCULOSIS

954. **Comparative Value of the Erythrocyte Sedimentation Rate, Electrophoresis, and the Haptoglobin Index in the Management of Pulmonary Tuberculosis.** (Valeur comparée de la vitesse de sédimentation de l'électrophorèse et de l'indice d'haptoglobine en phtisiologie)
A. ROULET, E. TRINQUIER, and S. ROULET. *Presse médicale* [*Presse méd.*] **63**, 355–357, March 9, 1955. 3 figs., 16 refs.

Samples of serum from 50 normal subjects, 90 tuberculous patients, and 10 patients with diseases other than tuberculosis were examined by paper electrophoresis, the erythrocyte sedimentation rate and haptoglobulin index being determined at the same time. The electrophoretic protein patterns in cases of quiescent tuberculosis were similar to those of normal subjects (albumin 57·4%, α_1 globulin 4·19%, α_2 globulin 7·66%, β globulin 12·37%, and γ globulin 18·16%), but differed significantly from those in cases of active tuberculosis (albumin 48·1%, α_1 globulin 4·96%, α_2 globulin 11·40%, β globulin 13·63%, and γ globulin 21·92%).

The authors conclude that although the erythrocyte sedimentation test is the simplest clinical test for use in the management of a tuberculous patient, it is the least reliable. The haptoglobulin index is more reliable, but is affected by any factor that affects the α_2-globulin value. Paper electrophoresis gives results similar to those that can be deduced from the haptoglobulin index, but has the additional advantage of giving a picture of all the serum globulins and thus information on the renal and hepatic state of the patient, which may be of the greatest value if surgical intervention is being considered.

J. E. Page

955. **The Treatment of Certain Forms of Pulmonary Tuberculosis with ACTH in Association with Antibiotics.** (Le traitement de certaines formes de tuberculose pulmonaire par l'association d'ACTH et d'antibiotiques)
J. LEDERER, P. MANNES, R. DERRIKS, and R. NICAISE. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **71**, 273–282, March 4, 1955. 20 refs.

The authors describe 4 clinically diverse cases of pulmonary tuberculosis which had failed to respond to, or had relapsed after, standard treatment with antibiotics, and which were given ACTH (corticotrophin). This treatment was, in their view, responsible for a favourable outcome in at least 2 cases, namely, one of miliary tuberculosis with meningitis and one of tuberculous bronchopneumonia; in both of these recovery began only when ACTH was given. They were particularly struck by the rapidity of closure of cavities, present in 3 of the cases, and the conversion of the sputum. ACTH was also of benefit in reducing drug hypersensitivity, although it failed in one case to control a rash due to streptomycin.

The authors recognize the considerable divergence of views on the value of ACTH in pulmonary tuberculosis. They agree that large doses are definitely dangerous, and in treating these 4 cases they limited the dosage to 5 to 10 mg. daily intravenously, or 5 to 20 mg. intramuscularly. Considerable stress is placed on the safety and clinical value of these minute doses, but they must of course always be supplemented with the usual antibiotic therapy. The hormone is best given continuously for a period of 6 to 12 weeks, and is to be preferred to cortisone.

The possible mode of action of ACTH is discussed at some length.

Paul B. Woolley

956. **Long-term Sequelae of Treatment with ACTH or Cortisone in Cases of Pulmonary and Pleural Tuberculosis.** (Suites éloignées de quelques traitements par l'ACTH ou la cortisone dans les tuberculoses pulmonaires et pleurales)
H. P. KLOTZ and A. GUEZ. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **71**, 361–380, March 18, 1955.

The authors report, from the Hôpital Bichat, Paris, the results of the treatment of 15 cases of pulmonary and pleural tuberculosis with ACTH (corticotrophin) or cortisone in addition to the usual antituberculous drugs. ACTH was given in a dose of 10 mg. by infusion over 6 hours in glucose saline, or in doses of 100 to 200 mg. intramuscularly twice daily; cortisone was given in a dosage of 25 to 50 mg. per day. The average length of each course was 10 days.

The 15 cases were divided into four groups according to the result of treatment: (1) 6 showed marked improvement in the tuberculous and general state; (2) 3 showed improvement in the local tuberculous condition; (3) in 4 no improvement occurred; and (4) in 2 cases there was improvement in some aspects of the disease, but deterioration in others. The 6 patients showing marked improvement did so rapidly, although the disease was widespread and all were gravely ill. The 3 showing only local change included 2 cases of serofibrinous disease. After administration of ACTH there was a pronounced diminution in the amount of fluid and considerable radiological improvement. Of the 2 cases undergoing only partial improvement, in one there were definite radiological signs of healing, but at the same time the general condition of the patient became worse after treatment. In the other there was a rise in temperature lasting 3 weeks after the first course of ACTH and another rise lasting 10 days after the second course of the hormone.

Summing up, the authors conclude that ACTH is probably most efficacious in cases of acute inflammatory disease and in patients with pyopneumothorax, although in the present series it was of most value as a means of arresting the spread of the disease. If the disease is very advanced these hormones have no influence on the final prognosis, although death may be delayed for a few months. They point out that hormonal treatment prevented the formation of adhesions in their cases of

serofibrinous tuberculosis, and was also of value in the management of cases with purulent effusion, the combined use of ACTH and chemotherapy preparing the way for surgery. ACTH by itself is of course not curative of tuberculosis, although it enhances the action of streptomycin, PAS, and isoniazid in most forms of the disease. *Thomas Marmion*

957. **The Treatment of Pulmonary Tuberculosis with Cyanacetic Acid Hydrazide.** (Die Behandlung der Lungentuberkulose mit dem Hydrazid der Cyanessigsäure (CEH))
H. ROTHE. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **113**, 174–184, 1955. 22 refs.

At the Medical Clinic of the University of Leipzig cyanacetic acid hydrazide was given in doses of 5 to 15 mg. per kg. body weight for 3 months to 18 patients with chronic pulmonary tuberculosis who had already been treated for long periods with other antibacterial drugs. No troublesome toxic effects were seen, but strains of tubercle bacilli resistant to the drug emerged during treatment; sensitivity to isoniazid, streptomycin, PAS, and thiacetazone, however, did not appear to be altered. The sputum was positive in 16 cases before treatment and in 14 after treatment. *J. R. Bignall*

958. **The Treatment of Pulmonary Tuberculosis with "Reazid".** (Die Behandlung der Lungentuberkulose mit Reazide)
P. BIEDERMANN. *Schweizerische Zeitschrift für Tuberkulose* [*Schweiz. Z. Tuberk.*] **12**, 70–80, 1955. 3 figs., 6 refs.

The author reports the results of the treatment of 76 patients suffering from pulmonary tuberculosis with "reazid" (hydrocyanic acid hydrazide). The drug was administered orally in doses of 5 to 8 mg. per kg. body weight. Apart from slight side-effects (urticaria, conjunctivitis, and gastro-intestinal disturbance) in 3 cases, the drug was well tolerated and the patients showed an improvement in their state of health. The best results were obtained in recent cases with infiltrative lesions or with cavitation. *Franz Heimann*

959. **The Treatment of Cough with D-Methorphan Hydrobromide ("Romilar") in Tuberculosis.** (Traitement de la toux avec le bromhydrate de dextrométhorphane ("romilar") en tuberculose)
G. CAPPELLO and S. DI PASQUALE. *Schweizerische Zeitschrift für Tuberkulose* [*Schweiz. Z. Tuberk.*] **12**, 80–88, 1955. 8 refs.

The sedative effect of "romilar" (D-methorphan hydrobromide) on dry and troublesome cough has been studied in 23 cases of pulmonary tuberculosis. Daily doses of 30 mg. were administered either orally or by injection for about 20 days; no evidence of addiction or intoxication was observed. The treatment reduced the number of coughing bouts and facilitated expectoration. Respiratory function tests before and after treatment showed the vital capacity and oxygen extraction index to be improved. *Franz Heimann*

960. **Isoniazid in the Treatment of Primary Tuberculosis**
R. M. TODD. *Lancet* [*Lancet*] **1**, 794–796, April 16, 1955. 10 refs.

The effect of isoniazid in the treatment of primary pulmonary tuberculosis in children was studied at Alder Hey Children's Hospital, Liverpool, 24 patients receiving 3 mg. per lb. (6·6 mg. per kg.) body weight daily in 3 equal doses for 3 months. Alternate cases were allocated to test and control groups in such a way as to give approximately equal numbers in three age groups—under 3, 3 to 6, and 7 to 13 years. In 43 cases the infection was regarded as having been present for less than 3 months—the period during which serious complications are most likely to follow primary infection. Four patients were admitted to hospital as the adult source case remained at home, the remainder being treated as out-patients. Rest in bed for 4 to 8 weeks was followed by gradual return to full activity, with some dietary supervision. All patients were seen monthly for 3 months and then at 3-monthly intervals, 46 continuing to attend for 12 months and some for nearly 3 years. In addition to the clinical findings, the child's vitality, appetite, and height and weight were recorded, and a chest radiograph taken. [Neither the leucocyte count nor the erythrocyte sedimentation rate was estimated.] In 2 of the treated patients (aged 6 and 7 years) a caseous gland ruptured into a bronchus about 6 months after the first visit, and the youngest control subject, who was under observation from the age of 16 weeks, developed tuberculous hip disease 18 months later. Apart from these, all the patients did well, there were no deaths, and no harmful effects of the drug were noted. The only statistically significant difference noted between the groups treated concerned patients aged 3 to 6 years, whose weight increased more quickly at first than that of the corresponding control group, while their *x*-ray findings appeared to clear more quickly in the first 3 months, although the latter difference was not significant when assessed on a statistical basis. The impression was gained, however, that isoniazid therapy was generally associated more often with a decrease in size of the primary lesion during the first 3 months, and although no difference was found between the two groups at the end of one year, the author suggests that if this impression of early improvement is correct, treatment with isoniazid might lessen the risk of complications. *A. White Franklin*

961. **Treatment of Tuberculosis with Intermittent Streptomycin and Isoniazid**
J. H. SCHAEFFER. *Antibiotic Medicine* [*Antibiot. Med.*] **1**, 153–157, March, 1955. 4 refs.

962. **Report of the Team Appointed by the Association of Swiss Tuberculosis Physicians on the Clinical Trial of "Rimifon" (Isoniazid).** (Erfahrungsbericht des Team der Gesellschaft schweizerischer Tuberkuloseärzte zur klinischen Prüfung von Rimifon)
B. FUST, G. WERNSDORFER, and W. WERNSDORFER. *Schweizerische Zeitschrift für Tuberkulose* [*Schweiz. Z. Tuberk.*] **12**, Suppl. 1, 1–344, 1955. 169 figs.

963. **Segmental Resection in Pulmonary Tuberculosis**
L. D. EERLAND and K. K. M. F. SEGHERS. *Diseases of the Chest* [*Dis. Chest*] **27**, 165–178, Feb., 1955. 6 refs.

A series of 285 patients with pulmonary tuberculosis who underwent segmental resection at the University Surgical Clinic, Groningen, Netherlands, between November, 1949, and August, 1953, is reported. All the patients were followed up for at least 6 months after the operation. Up to November, 1954, 490 segmental resections had been performed without mortality, the present series representing the first 300 such operations. The indication for operation was tuberculoma in 14·6% of the 300, caseous foci in 56%, cavitated disease in 20%, and failure of non-surgical collapse therapy in 9·33%. Only those patients were treated who had "quiet phthisic foci" which had not healed with bed rest and chemotherapy.

The surgical technique is outlined, the main points emphasized being the pleuralization of the raw lung surface by suturing together the edges and the burial of the bronchial stump beneath the pleura or in pulmonary tissue. Analysis of the segments resected showed that the apico-posterior segment of the left upper lobe was the one most frequently removed. Complications occurred in 127 cases, being classed as major in 78 and minor in 49. Among other conditions the former group included 6 cases of bronchopleural fistula, 8 of empyema, 24 of spread of infection, and 9 of reactivation. [The incidence of spread of infection appears to be high for cases which were selected for their apparent quiescence.]

The sputum became negative for tubercle bacilli in 292 cases immediately after operation, but reactivation had reduced this figure to 277 by the time of the report; 70% of the patients are back at work and there has been no late mortality. Postoperative pulmonary function studies indicated a greater loss than was to be expected in 49 cases, due in a number of these to phrenic paralysis.

In the final analysis the authors feel that 81% of the results can be classified as "good", 6% as "moderate", and 13% as "poor", the highest proportion of poor results and the lowest sputum conversion rate occurring in cases of cavitated disease. They point out, however, that as the figures become less good as time goes on, it is premature to pass any definite judgment on the operation of segmental resection at this stage.

A. M. Macarthur

964. **The Holst Type Thoracoplasty**
S. R. TAITZ and M. WALTON. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **48**, 217-221, July, 1954 [received Feb., 1955]. 5 figs., 2 refs.

Owing to apical re-expansion residual cavitation occurs in about 10% of cases in which upper thoracoplasty has been performed. To prevent this re-expansion, foreign bodies have been inserted to act as a plug. Holst, however, maintained apicolytic collapse with a dome thoracoplasty in which no extraneous material was used. In the present paper 54 Holst-type operations performed at Shotley Bridge Hospital, Newcastle upon Tyne, and Poole Hospital, Middlesbrough, between 1951 and 1953 are reviewed, the follow-up period varying from 6 to 32 months. All patients received preoperative chemotherapy and physiotherapy, and all were subjected to tests of respiratory function. The indications for operation were the same as for a standard thoracoplasty, but cases which showed cavitation at the apex of the lower lobe were excluded. Patients received a blood transfusion during the operation, which was carried out under general anaesthesia. [For details of the operative technique the original article should be consulted.]

One patient died from myocardial failure a few hours after operation. In 2 cases cavitation persisted under the Holst roof, and in 3 cases there was postoperative spread of disease. Pleural tears occurred in 27 of the 54 cases. Some of these were due to operative accident; they were closed if possible, or if not, an intercostal drain was inserted. In other cases the pleura tore on the rib ends, sometimes as long as 48 hours after operation, such tears being associated with haemopneumothorax. Aspiration was performed in these cases and to relieve the pressure caused by domal effusion. The wound was reopened in 2 cases because of infection of the space above the dome with *Staphylococcus aureus*. Paradoxical breathing occurred in 4 cases in the series. It is pointed out that with the fixed roof of the Holst operation paradoxical breathing should not occur, but that when it does it is due to failure of the fixation sutures to hold the roof in place.

Of the 53 patients followed up, the disease was quiescent and the sputum negative in 51. The authors claim that this one-stage procedure is mechanically sounder than two-stage thoracoplasty, collapse being obtained and maintained more easily. They hope that with further experience the high complication rate will be reduced.

Thomas Marmion

965. **A Study of Recurrence after Pulmonary Resection for Tuberculosis.** (Étude des récidives après résection pulmonaire pour tuberculose)
H. JOLY, J. TIRET, and J. VILLEMIN. *Poumon* [*Poumon*] **11**, 21–32, Jan., 1955.

Pulmonary resection for tuberculosis was performed on 130 patients at Passy Sanatorium, Paris, between 1949 and 1953. A follow-up study, extending over 6 months to 5 years and excluding those cases which had immediate postoperative complications, showed that 15 patients (11·5%) have since relapsed. In 9 cases there was recrudescence of the disease in previously existing lesions, new lesions developed in apparently healthy lung in 5 cases, and both recrudescence and fresh disease occurred in one case. Fresh disease usually appeared in the lower lobe of the same lung following resection of the upper lobe, and was probably due to over-distension; post-resection thoracoplasty was not performed in any of these cases.

The authors stress that prolonged rest in bed and a course of chemotherapy must precede and follow resection of the lung for tuberculosis, and their results in more recent cases, in which this procedure was followed, support this view.

S. F. Stephenson

See also Microbiology and Parasitology, Abstract 927.

Venereal Diseases

966. **The Etiology of Nongonococcal (Nonspecific) Urethritis**
R. R. WILLCOX. *Journal of Chronic Diseases* [*J. chron. Dis.*] **1**, 381–391, April, 1955. 42 refs.

Writing from St. Mary's Hospital, London, the author points out that the present high incidence of non-specific urethritis and the lack of precise knowledge of its aetiology render it urgent that the causative organism should be identified without delay.

Among the possible pathogens which have been considered are bacteria, trichomonads, spirochaetes, pleuropneumonia-like organisms (P.P.L.O.), and viruses. He has found little difference in the bacterial flora of the urethra in treated and untreated cases and in controls. *Trichomonas vaginalis* has been reported by various workers to be present in from 5 to 29% of cases, but the author feels that there is still insufficient evidence to incriminate *T. vaginalis* in the majority of cases, although the successful experimental inoculation of the male urethra with cultures of this organism in a small number of volunteers reported by Lanceley and McEntegart (*Lancet*, 1953, **1**, 668; *Abstracts of World Medicine*, 1953, **14**, 401) demands further research.

It has been suggested that spirochaetes similar in morphology to those found in the mouth may be of importance, as they are in abacterial pyuria, but an inquiry carried out by the author suggested that the practice of oral or anal coitus was no more frequent among patients with non-specific urethritis than in the general population. Much work has also been done recently on the relation of P.P.L.O. to non-specific urethritis, but these organisms have been found so often in healthy men and women that the author regards them as commensals.

The blue-staining inclusion bodies and red granules well known in the epithelial cells in trachoma have also been found in scrapings from the urethra of patients with so-called inclusion blennorrhoea and non-specific urethritis. The author has therefore attempted to obtain additional evidence for a viral aetiology of non-specific urethritis by means of dermal and serological tests. In a series of skin tests with antigens of the lymphogranuloma–psittacosis–trachoma group of viruses negative results were obtained with the psittacosis antigen, but with "lygranum" antigen and cat-scratch antigen positive results were slightly more frequent in cases of non-specific urethritis than in controls. Complement-fixation tests for lymphogranuloma venereum and for enzootic abortion in ewes (due to a similar organism) gave no significant results. Giemsa-stained urethral scrapings from a large number of patients, their female consorts, and from controls were examined for virus inclusion bodies, elementary bodies, and P.P.L.O. The author concludes that none of these bodies can be incriminated as the cause of non-specific urethritis. Finally, attempts to passage the virus or causal organism of non-specific urethritis into the brain or ungs o mice, subcutaneously into guinea-pigs, into the urethra, conjunctiva, or knee joints of baboons, or into embryonated hen's eggs were entirely unsuccessful. The cause of non-specific urethritis therefore still remains to be discovered.

V. E. Lloyd

967. **Follow-up Studies in Cardiovascular Syphilis**
F. KALZ and A. I. SCOTT. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **72**, 274–279, Feb. 15, 1955. 5 refs.

The authors, believing that "detailed studies of the life expectancy and the general prognosis of adequately treated patients should be of practical value", report their findings in 111 cases of cardiovascular syphilis treated previous to 1948 and followed up at the Royal Victoria Hospital, Montreal. Only 2 cases were lost to observation, 84 were observed for at least 5 years, 53 for 10 years, and 25 for 15 years. Altogether there were 46 deaths, by no means all attributable to syphilis. The frequency and causes of death are tabulated and discussed. The authors consider the following classification of cases of cardiovascular syphilis to be useful: (1) uncomplicated aortitis; (2) aortitis complicated by simple aortic insufficiency but without signs of coronary disease or congestive failure; (3) aortitis complicated by coronary involvement (with or without aortic insufficiency); (4) cardiovascular syphilis with congestive failure; and (5) saccular aneurysm. They find that with appropriate treatment Groups 1 and 2 have a favourable prognosis; in Groups 3 and 4 the prognosis is unfavourable regardless of the therapy given; while that in Group 5 depends on the degree of pathological change and the state of the coronary circulation. Over 30% of the saccular aneurysms met with terminated in rupture. The main conclusion of this study, therefore, is that prognosis depends on the presence or absence of either coronary arterial involvement or congestive failure.

The authors have omitted any details of sex, race, or age distribution, since it was impossible to establish any relative correlations in this small series.

Douglas J. Campbell

968. **Penicillin Treatment for Early Congenital Syphilis**
C. A. SMITH, G. A. GLEESON, and K. H. JENKINS. *Archives of Pediatrics* [*Arch. Pediat.*] **72**, 12–25, Jan., 1955. 2 figs., 4 refs.

The records of 472 cases of early congenital syphilis treated with penicillin alone during 1946–50 have been studied by the authors, working in the U.S. Public Health Service, Washington, D.C. Cases in infants under 3 months of age were included only when obvious clinical signs of infection were present in addition to a positive reaction to serological testing. Approximately 40% of the 472 patients had been followed up for 18 to

21 months; the authors appreciate that this period is far too short to provide any information regarding the adequacy of penicillin treatment in preventing the development of late clinical manifestations of congenital syphilis.

During the follow-up period 10 cases were classified as clinical or serological failures, though 4 of these received re-treatment on a " clinician's decision ", which on later review seems to have been unjustified. Nevertheless, 2 patients had re-treatment for serum resistance, 2 for clinical relapse, and one for serological relapse. In all 56 patients whose cerebrospinal fluid was examined in the post-treatment period normal results were obtained.

The authors conclude that in early congenital syphilis the pattern of serological behaviour after treatment is analogous to that in the early stages of acquired disease; also that when aqueous crystalline penicillin is used, best results are obtained with a dosage of 321,000 units or more per kg. body weight. A few of the patients were treated with penicillin in oil and beeswax with equally successful results. *G. L. M. McElligott*

969. **Study of the TPI Test in Clinical Syphilis. II. Comparison with the VDRL Slide Test in Treated Early Symptomatic Syphilis**
W. F. Edmundson, M. Kamp, and S. Olansky. *Archives of Dermatology* [*Arch. Derm.* (*Chicago*)] **71**, 384–386, March, 1955. 7 refs.

This report from the Venereal Disease Research Laboratory, Chamblee, Georgia, presents the results of a comparative study of the treponemal immobilization (T.P.I.) and V.D.R.L. slide tests, which were carried out in parallel on sera from 188 patients at varying periods after adequate treatment with penicillin for early syphilis. The T.P.I. test was not performed before treatment, nor were serial tests carried out.

In 77 cases the patient had been treated for primary syphilis 3 months to 4 years or more before the tests were performed. Sera from only 2 patients (treated respectively 3 months and one year previously) were reactive with the V.D.R.L. test, whereas 7 sera were reactive with the T.P.I. test (" reactive " including both positive and doubtful reactions). The interval since treatment was 3 months in 3 of these 7 cases, one year in one, 2 years in another, and 4 years in the remaining 2 cases. In one case the serum was reactive with the V.D.R.L. test a year after treatment, but gave a negative T.P.I. reaction.

The tests were also carried out on sera from 111 patients who had been treated for secondary syphilis, these being reactive with the V.D.R.L. test in 33 cases and with the T.P.I. test in 51. In about half the cases tested 3 months after treatment the serum was reactive with the T.P.I. test, but this proportion fell to one-quarter in the cases which were not tested until 4 or more years after treatment. The V.D.R.L. reaction had become negative one year after treatment in all but a few cases (7·4%), in 5 of which the T.P.I. reaction was negative.

This lack of correlation between the results of the two tests emphasizes the need for careful questioning of the patient about previous antisyphilitic treatment before attempting to interpret the result of either test in this type of case. *A. E. Wilkinson*

970. **A Quantitative Analysis of the Sachs–Witebsky Reaction on 1,146 Sera.** (Analisi quantitativa di 1146 sieri con la reazione di Sachs–Witebsky)
G. Lomuto. *Giornale italiano di dermatologia e sifilologia* [*G. ital. Derm. Sif.*] **96**, 43–70, Jan.–Feb., 1955. Bibliography.

Writing from the University Skin Clinic, Bari, the author points out the prognostic and therapeutic importance of a quantitative serological follow-up of syphilitic patients.

In the study here described 1,146 sera from 802 patients were examined by the Sachs–Witebsky (S.W.) reaction for lipid flocculating antibody, and 24 hours later the quantitative reaction of the positive sera was determined. The technique used is briefly outlined. The same pipette was used for all tests, and re-inactivation of the serum for the quantitative test is not necessary. It was unfortunately not possible to shorten or simplify the quantitative reaction to such an extent as to render it practicable for routine application in place of the qualitative test.

The most important of the findings were as follows. Repetition of the test after 24 hours often shows a change in titre; in 17% of the present cases a decrease and in 3% an increase in titre occurred. The level of antibody is related to the stage of syphilis; it may be absent, or present at a titre of no more than 1 in 4, in primary cases, but is never below 1 in 4 in secondary cases; in clinically manifest tertiary syphilis the titre is usually lower than in secondary. In untreated congenital cases the titre is usually high and a zone phenomenon often occurs; this phenomenon, which the author defines as a stronger reaction at a higher dilution, although this does not imply a completely negative reaction in a lower dilution, is considered to be due to excess antibody and was observed in 50% of all untreated congenital cases in this series, while most other cases with zoning were long-standing cases.

Performance of the S.W. test with twice the normal amount of serum gave an attenuation of the reaction in 9 cases (probably due to zoning), but an increase in intensity in 68 cases, 6 of those which had been negative with a normal amount of serum becoming positive; the procedure is, however, not recommended. A strongly positive complement-fixation reaction is usually associated with a positive S.W. test result, but the reverse is not true. As an example of a non-specific reaction, 34 out of 60 samples of serum from patients with leprosy gave positive results, many with a high titre persisting over several dilutions.

The serological reactions in a number of cases was followed through a period of treatment with penicillin or with bismuth and arsphenamine. The titres were inconclusive, but the author inclines to the belief that penicillin lowers the titre less than the older forms of treatment in long-standing cases. In recent cases penicillin is superior. *F. Hillman*

Tropical Medicine

971. **The Treatment of Chronic Amoebic Dysentery with Antibiotics in Combination with Other Drugs**
I. SINGH. *Lancet* [*Lancet*] **1**, 527–528, March 12, 1955. 5 refs.

Treatment with a combination of chlortetracycline, carbarsone, di-iodohydroxyquinoline, and chloroquine for 6 days, followed without a break by di-iodohydroxyquinoline and chloroquine alone for 14 days, was given to 32 patients with chronic amoebic dysentery which had proved resistant to other forms of treatment. Only cases in which stool or sigmoidoscopic examination had given positive results were selected; 7 of the patients had associated hepatitis, one with clinical jaundice.

In 23 cases the symptoms subsided before or shortly after completion of the treatment. Diarrhoea continued for 6 to 14 days in 4 cases, being ascribed to the chlortetracycline in 3. In another case in which diarrhoea continued for 3 months rapid relief followed appendicectomy. In 5 cases in which colonic and caecal tenderness persisted this symptom was relieved by additional treatment with oxytetracycline, carbarsone, and mepacrine. All cases were considered to be cured at the end of 3 months on the basis of clinical, stool, and sigmoidoscopic examination, with tests for occult blood. Subsequent follow-up in 20 of the cases for periods of 8 months to 2 years confirmed that the cure was permanent.

R. R. Willcox

972. **Malaria and the Sickling Trait**
A. B. RAPER. *British Medical Journal* [*Brit. med. J.*] **1**, 1186–1189, May 14, 1955. 9 refs.

The author has studied resistance to malarial infection in relation to possession of the sickling trait in 3 groups of African subjects: (1) 1,200 children under the age of 10 years attending the out-patient department of Mulago Hospital, Kampala, Uganda, for a variety of reasons; (2) 1,194 children under 5 years of age attending child welfare clinics in and around Kampala; and (3) 663 mothers of children in Group 1. In Groups 1 and 2 the gross malarial parasite rate was lower in those with the sickle-cell trait, but not significantly so, while in Group 3 it was higher, but again the difference was not significant. In Group 1, however, infections with the different species of parasite were considered separately, when it was found that the incidence of infections with *Plasmodium falciparum* was significantly lower in those with the trait, whereas infection with *P. malariae* did not appear to be affected. Moreover, parasite counts in children with *P. falciparum* infections were much lower in the presence of the sickling trait.

Although these findings confirm those of Allison (*Brit. med. J.*, 1954, **1**, 290) that possession of the sickling trait confers some protection against *P. falciparum* malaria, the present author's view is that the presence of sickle-cell haemoglobin does not prevent infection with the plasmodium, but limits the extent of its development so that the attack is briefer, less disabling, and less dangerous.

J. A. Sinclair

973. **Effect of Sickle-cell Trait on Resistance to Malaria**
E. BEUTLER, R. J. DERN, and C. L. FLANAGAN. *British Medical Journal* [*Brit. med. J.*] **1**, 1189–1191, May 14, 1955. 6 refs.

The authors, working at the U.S. Army Malaria Research Unit, University of Chicago, have studied the effect of possession of Type-S (sickle) haemoglobin on resistance to malaria under carefully controlled conditions. The subjects, 16 American negroes who had never previously had malaria, were volunteers drawn from inmates of a prison, and comprised 8 with the sickle-cell trait whose blood contained both normal and sickle haemoglobin and 8 normal subjects whose blood contained only normal haemoglobin. In each experiment the subjects were inoculated with aliquots of a single freshly drawn sample of heparinized, Group-O, Rh-negative blood infected with trophozoites of *Plasmodium falciparum*. The infection was terminated with chloroquine when it became necessary for the patient's safety, the longest period before treatment was instituted being 23 days after inoculation. In the first experiment 5 members of each group were inoculated with 500,000 parasites each; in the second the remaining 3 in each group were given an injection of blood containing only 50,000 parasites; and in the third the 10 subjects of the first experiment were re-inoculated with 50,000 parasites after a lapse of 4 months.

The authors were unable to find any impressive differences in the resistance between the subjects with and without the sickle-cell trait, their results thus failing to confirm those of Allison (*Brit. med. J.*, 1954, **1**, 290). A possible explanation is that the authors used a Panamanian strain of *P. falciparum* whereas Allison used African and Malayan strains. Also the latter's subjects were highly immune, while only in the last experiment were the present authors' subjects slightly immune, and it is possible that the sickle-cell trait confers protection only when a high degree of acquired immunity already exists [see also Abstract 972].

J. A. Sinclair

974. **Toxicity Studies of Pyrimethamine (Daraprim)**
R. J. DERN, E. BEUTLER, J. ARNOLD, A. LORINCZ, M. BLOCK, and A. S. ALVING. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **4**, 217–220, March, 1955. 4 refs.

The administration of pyrimethamine ("daraprim") to 81 men in doses of 25 mg. weekly for 6 months failed to produce toxic effects. In 133 other men, who received the drug as malaria therapy on various schedules, no toxic effects which could be unequivocably attributed to pyrimethamine were observed.—[Authors' summary.]

Nutrition and Metabolism

975. **Studies in Iron Transportation and Metabolism. VIII. Absorption of Radioiron from Iron-enriched Bread**
R. STEINKAMP, R. DUBACH, and C. V. MOORE. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 181–193, Feb., 1955. 7 figs., 15 refs.

The value of fortifying flour with iron was investigated at Washington University School of Medicine, St. Louis. Four preparations commonly used for this purpose—ferrous sulphate, reduced iron, ferric orthophosphate and sodium ferric pyrophosphate—were made from radioactive iron (^{59}Fe) of high specific activity (1,710 μc. per mg.) and each was added to flour which was then baked into bread according to normal bakery practice. The bread was eaten in the morning after an overnight fast by 26 healthy male medical students, 6 healthy women, and 3 patients with hypochromic anaemia. The faeces of all subjects were collected for measurement of the unabsorbed radioactivity, and samples of blood were taken for estimation of the iron content of the erythrocytes.

The healthy subjects absorbed and utilized between 1 and 12% of the preparation added to the bread. No differences in this respect were observed between the various forms of iron used, but the authors point out that the baking process converts some of the ferrous sulphate to the ferric state. When a supplement of ascorbic acid was given to 6 healthy subjects their absorption of iron was two or three times that previously recorded. The iron-deficient patients absorbed 45 to 64% of the iron ingested in the bread.

It is concluded that iron added to bread makes a significant contribution to human nutrition. The fact that in this investigation metallic iron was as well utilized as the three iron salts leads the authors to recall the suggestion of Nakamura and Mitchell (*J. Nutrit.*, 1943, **25**, 39) that an important source of iron in the diet is supplied by particles of the metal from iron milling machines. *I. McLean Baird*

976. **Tongue Appearance and Serum Albumin Level in the Assessment of Nutritional Status, with Reference to the Effects of a Protein-rich Diet**
B. GANDEVIA and D. HOSSACK. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 344–346, March 5, 1955. 7 refs.

The purpose of the investigation here reported from the Royal Melbourne Hospital, Melbourne, was to determine the relation between the dietary intake of protein and the appearance of the tongue and the serum albumin level. The subjects were two groups of students, men and women, one group (24) living at home and the other (16) living in institutions where the food was cooked in bulk. An inspection was made of the tongue, the appearance of which was classified in the manner suggested by Bolton (*Med. J. Aust.*, 1955, **1**, 10) according to the degree and distribution of atrophy or hypertrophy of the papillae. In addition, the total plasma protein, serum albumin, and haemoglobin levels were determined and, in the case of the "home students", a dietary history taken. The diet of the "institution students" was not analysed, but had been estimated previously to contain about 46 g. of animal protein daily. The institution students were then asked to eat a high-protein diet during a 2-week vacation at home, and the examination repeated on their return.

The first examination showed that the home students, whose daily intake of animal protein ranged between 42 and 112 g., had fewer abnormalities in tongue appearance and a higher average serum albumin level than the institution students, but on re-examination after 2 weeks' protein-rich diet the latter showed no significant difference in these respects from the home students. On the other hand the level of haemoglobin, which had previously been the same in the two groups, was significantly lower on re-examination in the group living in institutions.

Statistical analysis of these findings shows that it is possible, by assessing tongue appearance and the serum albumin level, to distinguish between groups of different nutritional status in respect of protein, although the scatter of the individual results makes it impossible to determine the status of any one person in this way. The estimation of the total serum protein level on the other hand has little or no value for this purpose. The reason for the fall in the haemoglobin level observed in the institution students after taking a high-protein diet is not clear, though it may have been brought about by haemodilution. *John Yudkin*

977. **Essential Pentosuria**
F. V. FLYNN. *British Medical Journal* [*Brit. med. J.*] **1**, 391–395, Feb. 12, 1955. 6 figs., 38 refs.

The use of paper chromatography to identify the urinary reducing substance in cases of apparent renal glycosuria led to the discovery of 2 cases of essential pentosuria at University College Hospital, London, in the course of 4½ years. The sugar was identified in both instances as xylulose. The cases are here described and the topic of essential pentosuria is briefly reviewed. Essential pentosuria is characterized by the constant excretion of small amounts of L-xylulose and has to be distinguished from alimentary pentosuria, in which arabinose or xylose is found in the urine after ingestion of a large amount of fruit or fruit products, and possibly also from ribosuria, which has recently been stated to occur in some cases of muscular dystrophy. Essential pentosuria is a harmless condition which, once discovered, can be shown to persist throughout the remainder of the patient's life, though it has never yet been proved to exist from birth. *K. O. Black*

Gastroenterology

978. **Socio-economic Distribution of Cancer of the Gastrointestinal Tract in New Haven**
E. M. COHART and C. MULLER. *Cancer* [*Cancer (N.Y.)*] **8**, 379–388, March–April, 1955. 5 refs.

This report, the third in a series prepared in the Department of Public Health of Yale University School of Medicine, deals with the socio-economic distribution of cancer of the oesophagus, colon, rectum, and pancreas in New Haven, Connecticut. The data were obtained from the files of the Connecticut State Cancer Register for the years 1935 to 1949 and from death-certificate records. The socio-economic status of each subject was determined from the place of residence, the various residential districts of the town having been aggregated into three broad groups according to the average economic status of the inhabitants.

No significant correlation was observed between economic status and the incidence of cancer of the rectum or pancreas, and this is in accord with findings in England and Wales and (so far as the rectum is concerned) in Denmark. The incidence of cancer of the colon was slightly above the average among women in the well-to-do districts, and this is in accord with the findings in Denmark. Both in England and Wales and in Denmark there has been reported an excess of cancer of the oesophagus among the poorer classes of both sexes, but the New Haven data provided only slight evidence of such a trend, and then only in men. Completeness of registration, reliability of diagnosis, stage of disease on admission to hospital, and 5-year survival rate did not appear to be related to socio-economic status.

Richard Doll

979. **Smoking and Chewing of Tobacco in Relation to Cancer of the Upper Alimentary Tract**
L. D. SANGHVI, K. C. M. RAO, and V. R. KHANOLKAR. *British Medical Journal* [*Brit. med. J.*] **1**, 1111–1114, May 7, 1955. 3 figs., 16 refs.

While oral cancer is relatively common throughout India, the commonest site of its occurrence within the mouth differs in the various localities and communities. The present work was undertaken primarily to see whether differences in the prevalence of chewing and smoking tobacco could account for the variation in site distribution.

A questionary was completed for 1,460 patients who first attended the Cancer Clinic of the Tata Memorial Hospital, Bombay, during the period 1952–4. Analysis of the data so obtained showed that both for men and for women those patients who were free of cancer and those with cancer other than in the upper alimentary tract included similar proportions who habitually smoked or chewed tobacco, but that among patients with cancer of the buccal mucosa, other parts of the oral cavity, oesophagus, hypopharynx, base of the tongue, and oropharynx the habits of smoking and chewing were more common. The number of cases occurring in women were insufficient for further analysis, but among men separate analyses could be made for 3 age groups and 4 community groups (Hindu Deccani, Hindu Gujarati, Muslim, and others). Comparison of the proportions of men who smoked and who chewed among those with cancer of each of the sites enumerated above with those among patients with cancer of other sites and among patients without cancer (after making allowance for differences in representation of the various age groups and communities) showed that the habit of chewing was strongly associated with cancer of the buccal mucosa and of other parts of the oral cavity, that the combined habit of smoking and chewing was associated with cancer of the hypopharynx and base of tongue, and that the habit of smoking was associated with cancer of the oropharynx and (to a lesser extent) of the oesophagus, whereas there was no association of these habits with cancer of other sites. Moreover, it was found that the average number of " bidis " smoked per day was greatest in patients with cancer of the hypopharynx, base of tongue, and oropharynx. (The " bidi " is a cigarette made by rolling tobacco flakes in the dried rectangular leaf of another plant. In Western India betel nut and betel leaf, which may be prepared with slaked lime, catechu, and spices, are used in addition to tobacco for chewing.)

These findings indicate that tobacco may be one of the environmental factors responsible for cases of cancer of the upper alimentary tract in India, although other factors are also likely to be contributory. Differences in chewing and smoking habits partly explain differences in incidence of cancer of the buccal mucosa and of the base of the tongue between Deccanis and Gujaratis. Genetic differences in tissue susceptibility may be one of the reasons why smoking appears to affect the mucosa of the upper alimentary tract in one population and of the lung in another, while differences between bidis and ordinary cigarettes in the physical state and internal dispersal of smoke particles may be another factor.

Richard Doll

980. **Pancreatitis following Pregnancy**
R. A. JOSKE. *British Medical Journal* [*Brit. med. J.*] **1**, 124–128, Jan. 15, 1955. 4 figs., 35 refs.

Six cases of pancreatitis following pregnancy admitted to the Royal Melbourne Hospital, Victoria, are described. In all of them the clinical and laboratory findings were similar. The possible aetiology of the condition is discussed and although the author regards pancreatitis following pregnancy as a distinctive syndrome, no causal connexion between the two conditions could be found. It is suggested that the term " post-partum pancreatitis " should be applied to such cases. *R. Schneider*

PHARYNX AND OESOPHAGUS

981. **Clinical Problems Associated with Esophageal Diverticula**
E. D. PALMER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 16–21, Jan., 1955. 4 figs.

In only 9 of 33 patients studied by the author at the Walter Reed Army Hospital, Washington, D.C., with diverticulosis of the oesophagus—hypopharyngeal, mid-thoracic or epiphrenic—did it cause any symptoms, the lesion being discovered by chance in the remaining 24 cases during the investigation of some other condition. Surgical treatment proved necessary in only 4 of the former. In 12 of the latter, however, the presence of the diverticulum interfered seriously with diagnosis or treatment by preventing the passage of a gastroscope or stomach tube. [The relative importance of this secondary clinical role forms the central theme of this short article, which scarcely touches on symptomatology or treatment and does not discuss aetiology or pathology.]
M. Meredith Brown

982. **Non-specific Oesophagitis**
K. V. LODGE. *Thorax* [*Thorax*] **10**, 56–57, March, 1955. 11 refs.

Non-specific oesophagitis is discussed with particular reference to its clinical importance. The study is based on the necropsy findings on 500 general hospital patients and 100 cases of sudden death. The relative frequency with which oesophagitis occurs in patients confined to bed is shown by its incidence of 36% in the hospital series of cases, and is contrasted with an incidence of only 8% in the " sudden death " series.

The importance of reflux of gastric contents in the aetiology of the disease is illustrated by the particular tendency of oesophagitis to occur in patients with severe vomiting or in whom prolonged gastric intubation is required. The effect of the horizontal posture and weakness of the diaphragmatic musculature in producing a similar reflux in bed-ridden patients is stressed. The frequent clinical silence of oesophagitis is noted. A correlation between clinical and necropsy findings, at present inadequate, is required to facilitate early diagnosis of the disease. Shortening and stricture of the oesophagus are noted as possible sequelae of the more severe lesions.

It is stressed that oesophagitis is a complication worthy of preventive measures by the general physician and general surgeon.—[Author's summary.]

983. **Achalasia of the Cardia in Adolescents Presenting with Respiratory Symptoms**
D. DAVIES and J. C. ROBERTS. *Lancet* [*Lancet*] **1**, 840–841, April 23, 1955. 5 refs.

The authors point out that, particularly in children and adolescents, the interference with swallowing that is normally characteristic of achalasia of the cardia may pass almost unnoticed. When this happens the patient when first seen may present evidence of respiratory disease which, however, is in fact secondary to a spill-over of the oesophageal contents into the bronchial tree from a dilated, food-containing oesophagus and which responds to treatment of the causative achalasia. In this short paper from Harefield Hospital, Middlesex, the authors draw attention to this possibility and give three illustrative case histories of patients aged 13, 14, and 18 respectively in whom this occurred. The diagnosis and treatment are briefly discussed.
T. A. A. Hunter

984. **A Review of 70 Cases of Hiatal Hernia, with Particular Reference to Symptomatology**
G. V. HALL and N. C. NEWTON. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 449–454, March 26, 1955. 7 figs., 5 refs.

The authors review the symptomatology, diagnosis, and treatment of hiatal hernia on the basis of their experience in 70 consecutive cases in 19 male and 51 female patients whose ages ranged from 26 to 82 years. They point out in particular the risk of confusing the chest pain of hiatal hernia with that of cardiac disease, and the fact that the hernia may be overlooked on radiological examination. *Norman C. Tanner*

STOMACH AND DUODENUM

985. **Haematemesis, with Special Reference to Peptic Ulcer**
G. J. FRAENKEL and S. C. TRUELOVE. *British Medical Journal* [*Brit. med. J.*] **1**, 999–1002, April 23, 1955. 2 figs., 7 refs.

The authors have studied 540 emergency cases of haematemesis or melaena admitted to the Radcliffe Infirmary, Oxford, in the 5-year period 1948–52 and compared them with the 305 cases admitted in the previous decade.

The over-all fatality rate in the later series (8·3%) showed a sharp decline from that in the earlier one (19·0%); and for cases of chronic peptic ulcer—numbering 377 in the present series—the mortality fell from 18·8 to 5·6%. In the present series 85·4% of the admissions were for acute or chronic peptic ulceration, 4·3% for bleeding oesophageal varices, and 3·7% for gastric carcinoma. One-third of the patients with a chronic ulcer had recurrent bleeding after admission, but the incidence of this bore no relationship to the length of history of ulcer, the age of the patient, or a history of previous haematemesis. In the peptic ulcer group 70% of the patients made an uneventful recovery, without further bleeding, under orthodox medical treatment; in this respect there was only a slight difference between the under-50 and the over-50 age groups (73·1% and 65·2% respectively). Of the 461 patients with acute or chronic peptic ulcer, 76 were treated by emergency partial gastrectomy with a mortality of 7 (9·2%), none of these deaths occurring in the under-50 age group.

The authors discuss the role of emergency surgery in the treatment of haematemesis and the causes of the decrease in the fatality rate, concluding that " a major cause of the improvement has been the more frequent resort to surgery ". *J. Warwick Buckler*

986. Peptic Ulcer Management with JB 323 (Piptal), a New Anticholinergic

J. A. RICSE. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **23**, 223–227, March, 1955. 7 refs.

"Piptal" (JB 323; N-ethyl-3-piperidyl-benzilate methobromide) is a postganglionic depressant similar in its action to atropine. In a trial of this drug at the Jersey City Medical Center, New Jersey, doses of 5 to 10 mg. were administered to 26 patients with duodenal ulcer, 5 with gastric ulcer, and 6 with hypertrophic gastritis. There was unequivocal relief from pain in 35 of the 37 cases. Of the other 2, one showed radiological evidence of healing, although pain was complained of throughout therapy with piptal and several antacids, and the other suffered from vomiting during treatment with piptal, which was attributed to his duodenal ulcer. In all of 6 patients given a barium meal for fluoroscopic examination before and after administration of piptal the emptying time was prolonged. The effect of the drug on gastric volume and free acid secretion was variable, some patients showing a marked decrease in both values, while in others there was little change.

[Details of the duration of treatment and follow-up are not given.] *Robert Hodgkinson*

987. Gastroduodenal Ulcer in Childhood with Bilateral Inheritance. (Ulcère gastroduodénal à début juvénile avec hérédité ulcéreuse double dans les lignées paternelles et maternelles)

M. LEVRAT, F. LARBRE, and M. RICHARD. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **43**, 1001–1010, Nov., 1954. 11 refs.

The authors describe 3 cases of duodenal ulcer, with onset in adolescence, in which there was a history of duodenal ulcer on both sides of the family. The first patient, a girl, had symptoms from the age of 12 and was found to have a duodenal ulcer with pyloric stenosis at the age of 19. In the second case, also in a girl, symptoms appeared at the age of 12 and duodenal ulcer was diagnosed the following year. The third, a man, had had symptoms since the age of 17, the presence of a duodenal ulcer being confirmed at the age of 28.

The family history of the first patient showed that the father had had a perforated duodenal ulcer at the age of 47, after 20 years of "indigestion", and that one of the mother's 2 brothers had also suffered from duodenal ulcer. The second patient had, on the mother's side, an aunt who had had an operation for peptic ulcer, an uncle who had a peptic ulcer, and another uncle who died at the age of 36 of haematemesis; on the father's side, an uncle of the patient had suffered from a duodenal ulcer from the age of 12. The third patient's father had symptoms of duodenal ulcer from the age of 33 and underwent a partial gastrectomy in 1941; his mother developed an ulcer in the pyloric region with symptoms from the age of 22, for which a gastroenterostomy was performed in 1936. The authors cite a number of other cases in which the early onset of peptic ulcer was associated with a history of ulcer on both sides of the family. *C. O. Carter*

988. The Practical Value of Histopathological Classification of Gastric Carcinoma. An Appraisal Based on 100 Consecutive Cases

E. R. FISHER and S. O. HOERR. *Cancer* [*Cancer (N.Y.)*] **8**, 389–395, March–April, 1955. 10 figs., 9 refs.

The authors present a survey of 100 cases of carcinoma of the stomach treated by gastric resection at the Cleveland Clinic, Cleveland, Ohio, and followed up for 18 months postoperatively. Each case was classified in one of five groups according to the histological type of carcinoma and was also graded simply according to the presence or absence of metastases and the degree of invasion of the stomach wall. As expected, the earlier the diagnosis and treatment, the better the prognosis. From this small series it appeared that scirrhous carcinoma, which is not readily diagnosed from gross appearances, carries the worst prognosis, and for this type of tumour the authors advocate total gastrectomy and wide resection of lymph nodes. It is suggested that histopathological classification of the tumour, as described, is of practical value in predicting the outcome in these cases.

[It is difficult to draw any firm conclusions after such a short follow-up period, but the number of cases considered by the authors as suitable for radical surgery is higher than that encountered in similar reported series.] *Roland N. Jones*

LIVER

989. Studies of Hepatic Function in Diabetes Mellitus, Portal Cirrhosis and Other Liver Diseases. A Correlation of Clinical, Biochemical and Liver Needle Biopsy Findings

A. BOGOCH, W. G. B. CASSELMAN, A. KAPLAN, and H. L. BOCKUS. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 354–384, March, 1955. 11 figs., bibliography.

A study designed to provide information about the liver in diabetic subjects was undertaken jointly at the Graduate Hospital, University of Pennsylvania, and the Banting and Best Department of Medical Research, University of Toronto. Clinical and biochemical investigations were carried out in 16 cases of diabetes mellitus with reference to liver function, and the results compared with those obtained in 17 cases of liver disease without diabetes, the latter including 7 cases of portal cirrhosis. At the same time that blood was taken for biochemical examination a needle biopsy of the liver was performed in order to correlate the biochemical findings with histological and histochemical changes. In all, 17 biochemical tests were carried out on the blood of these patients. Histochemical staining of hepatic tissue was used to demonstrate the presence of glycogen, deoxypentose nucleic acid, pentose nucleic acid, various lipids, and haemosiderin. No correlation was found in any of the cases examined between the serum lipid level and the quantity of lipid demonstrable histochemically in the liver, or between the blood glucose level at the time of biopsy and the amount of glycogen in the liver. Similarly the absence of correlation between the results of flocculation tests and the histological findings was demonstrated once more, as was the variability of the

histological findings in different parts of a biopsy specimen. No biochemical, histological, or histochemical change characteristic of the diabetic state was noted in the liver.

[This careful study should be read by anyone who undertakes the formidable task of trying to correlate the severity of a biochemical "lesion" as demonstrated by liver function tests with that of a morphological lesion demonstrated histologically—histochemistry being an attempt to bridge the gap. The difficulty lies in trying to detect in a static microscopical section what is essentially a dynamic process.] *G. S. Crockett*

990. **Postnecrotic Cirrhosis of the Liver. A Study of Forty-five Cases**

O. D. RATNOFF and A. J. PATEK. *Journal of Chronic Diseases* [*J. chron. Dis.*] **1**, 266–291, March, 1955. Bibliography.

It has gradually become recognized that a type of cirrhosis distinct from the more common Laennec's variety, and best described as postnecrotic cirrhosis, follows acute necrosis of liver cells from various causes which is insufficient in amount to cause rapid death from hepatic failure, but results in a combination of regeneration (nodular hyperplasia) and extensive fibrosis or scarring. It is true, however, that in a number of instances the post-mortem changes do not permit the condition to be clearly classified in either category. In animal experiments—all on rats and similar small animals—both types of lesion have been produced; but these animal experiments have not so far been shown to be directly applicable to human pathology. Suggestions for prophylaxis have been made, but once the lesion is established and fibrosis has occurred, cure is not possible.

To obtain a clearer understanding of its natural history the authors have made a most careful and elaborate study of 45 cases of postnecrotic cirrhosis collected from three hospitals in Baltimore, Cleveland, and New York. They point out rightly that this type of cirrhosis is much less common than the Laennec type and has a much wider age incidence, and in their series it was commoner in women than men. A careful review of aetiological factors shows the most frequent to be acute infective (viral) hepatitis (12 out of the 45 cases appeared to begin in this way), but many other hepatotoxic factors may be involved. [The abstracter has seen a group of cases following T.N.T. poisoning in young women employed in filling shells in the first world war, and also several following at an interval after typhoid fever.] Alcohol appeared to be an essential factor in only 13 patients out of the 45 studied.

The general symptomatology, course, and prognosis are discussed at length, but are not greatly different from those of any other type of established cirrhosis. In the present series 27 patients died of gradual hepatic failure or cholaemia, and gastro-intestinal haemorrhage was common. Primary carcinoma of the liver is generally thought to be more frequent in postnecrotic cirrhosis than in the Laennec type, but since all cases complicated by neoplasm were excluded from the authors' series no evidence is provided on this point.

[The authors' admission that "there are many gaps in our knowledge about this disease" is pertinent; and animal experiments have not so far helped very much. There is a very extensive bibliography, but the references are mainly to papers published in the U.S.A.] *J. W. McNee*

991. **Blood-ammonium Levels in Liver Disease and "Hepatic Coma"**

E. A. PHEAR, S. SHERLOCK, and W. H. J. SUMMERSKILL. *Lancet* [*Lancet*] **1**, 836–840, April 23, 1955. 5 figs., 17 refs.

In cirrhosis of the liver the administration of large doses of ammonium chloride has led to the development of neurological complications, and an attempt has been made at the Postgraduate Medical School of London to assess the usefulness of blood ammonium estimation as a routine clinical procedure in this disease. To this end 350 estimations of the blood level of ammonium have been performed on 66 patients with liver disease, 33 of whom had neurological signs varying from minor disturbances of consciousness or tremor to coma, and on 33 healthy subjects.

There was fair correlation between the blood ammonium concentration and the degree of neurological disability, although 10% of the values in patients with neurological signs were within normal limits. Blood ammonium levels over 2 μg. per ml. (twice the upper limit of normal) were always associated with neurological signs. Serial estimations in the same patient showed considerable fluctuations which could not always be related to changes in clinical status.

The Conway technique, which was used throughout the investigation, was found to be of uncertain specificity and technically difficult, as ammonium is liberated from the blood after it has been shed, so that timed pipetting of blood into the Conway chamber must be done at the bedside. Therefore the authors cannot recommend this test for routine use in the diagnosis of the neurological complications of liver disease or in assessing prognosis. *P. C. Reynell*

992. **Studies in Portal Hypertension: Estimated Portal Pressure and Hepatic Blood Flow in Patients with Cirrhosis of the Liver and Other Disorders**

A. W. T. EDWARDS. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 671–676, May 7, 1955. 25 refs.

In describing an investigation at the Royal Prince Alfred Hospital, Sydney, the author stresses the value of estimating the portal pressure in liver disease and makes a plea for "the earlier and more logical selection of patients for shunt operation". Catheterization of the hepatic vein was carried out on 23 patients, 17 of whom had cirrhosis of the liver, portal venous pressure being estimated by the occluded catheter technique and hepatic blood flow by the "bromsulphalein" clearance method. Of the 17 patients with cirrhosis, 9 had significant portal hypertension, and it is noteworthy that in the majority of these biopsy showed maximum distortion and fibrosis of the liver. Hepatic blood flow was within normal limits in 6 of the 7 patients with cirrhosis in whom this was estimated. *P. C. Reynell*

INTESTINES

993. The Difficult Appendix. Physiology Applied to Diagnosis

J. A. KERR. *Lancet* [*Lancet*] **1**, 736–740, April 9, 1955.

In the course of an attack of acute appendicitis there is often a latent period when signs and symptoms are few and minimal; in order to avoid mistakes it is essential always to pay serious attention to any history of recent acute abdominal pain. The symptoms of appendicitis vary greatly according to the anatomical position of the appendix. Inflammation of a retrocaecal or paracaecal appendix causes local irritation of the parietes, of the psoas muscle, or of the caecum itself, while an inflamed appendix in the pelvis causes no rigidity of the abdominal wall, although it can usually be diagnosed by careful rectal examination.

The author [rightly] calls attention to the difficulty encountered in diagnosis when the inflamed appendix lies behind the end of the ileum and is tethered by a short meso-appendix. Parietal irritation and local tenderness may be minimal, and the lower ileum, irritation of which at first causes frequent, small motions, may later be paralysed owing to sub-ileal peritonitis. As the peritonitis spreads, so does the local tenderness, while the general symptoms increase. This sequence of bowel irritation followed by local ileus is said to be characteristic of acute inflammation of an appendix of this type. Seven illustrative clinical cases are described.

[This article is not easily summarized in a few sentences, but well repays study.] *Zachary Cope*

994. Ulcerative Colitis. Follow-up Studies

F. C. WHEELOCK and R. WARREN. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 421–425, March 17, 1955. 7 refs.

The authors endeavoured to ascertain the fate of all patients treated for ulcerative colitis at the Massachusetts General Hospital, Boston, from 1915 to 1943. These numbered 483, of whom 343 were traced for at least 10 years or until death.

Of the 343 patients, 188 (54·7%) had died—153 of ulcerative colitis and 35 from other causes. Of the patients who had died from colitis, 46 had been treated medically and 107 surgically. Although only 155 (45·3% of the 343) were still alive, it is possible that a higher proportion of the untraced patients survived. It was known that at least 232 (48%) of the total of 483 cases came to operation sooner or later. Of the 196 surgical cases in which the duration of disease before operation could be established, 64 (32%) were operated upon within a year of onset and the remainder after varying lengths of time; in 62 (31%) the disease had been present for more than 5 years at the time of operation. Of the 155 survivors, 64 (79%) of the 81 treated medically and 70 (94%) of the 74 operated upon remained well. Carcinoma of the large bowel developed in 28 (8·8%) of the 319 patients who lived 10 or more years after the onset of the disease without undergoing colectomy. It is noted that 6 of this last group had never been ill enough to be admitted to hospital. Subsequent obstruction of the small bowel occurred in 18 cases, necessitating admission to hospital on 26 occasions; 4 of the patients died. In all except one of these 18 cases of obstruction the first attack took place within one year of operation.

[This paper merits careful reading by all interested in the problem of ulcerative colitis. It is unfortunate that there is no indication of the number of patients given out-patient treatment only, nor of the number who were admitted during the first attack or were referred from elsewhere. This last group may be partly responsible for the high proportion of cases treated surgically, particularly among those with a long history.]

T. D. Kellock

995. Ulcerative Colitis Treated by Total Colectomy and Ileo-rectal Anastomosis

S. AYLETT. *British Medical Journal* [*Brit. med. J.*] **1**, 1060–1062, April 30, 1955. 2 refs.

In a previous paper (*Brit. med. J.*, 1953, **2**, 1348) the author described an operation of ileo-rectal anastomosis with colectomy which he claims can be carried out in all cases of ulcerative colitis where surgery is indicated, except those in which the rectum has been irretrievably damaged by gross fibrosis or by perirectal suppuration and fistula formation. He now describes certain modifications in surgical technique and records the progress of patients who have undergone the operation at the Gordon and Metropolitan Hospitals, London.

In the earlier cases the ileum was anastomosed to the rectum in its upper third and the distal sigmoid brought out in the left iliac fossa to act as a safety valve, the mucous fistula being excised later. In more recent cases the rectum has been mobilized in the initial stages of the operation and the total excision carried down to within 2 cm. of the anastomosis, the upper end of the rectal stump being then brought out at the lower end of the paramedian incision. It is claimed that with this technique surgical closure of the fistula is less often required than when the distal colon is used as a safety-valve. A table summarizing the results of the operation in 17 cases is given, together with an addendum including a further 6 cases. Among the total of 23 cases only one death has occurred—the result of a "burst abdomen" 4 weeks after operation. The majority of the patients were operated upon in one stage; some were acutely ill and in a fulminating phase of the disease.

Apart from improving the general health and nutrition of these patients, the operation has left them with a continent sphincter. In the most favourable cases there have been as few as 3 bowel actions during the daytime and one at night; while at the other end of the scale were 8 to 9 actions in the day and 2 to 3 at night (in one case). It would seem that, on the average, 4 to 6 actions of the bowel during the day with an occasional one at night is a result that can confidently be expected.

A warning is given that it would seem to be wise to resist any temptation to preserve an apparently healthy caecum. Two further cases, in one of which the patient ultimately died, are summarized to give point to this.

C. Patrick Sames

Cardiovascular System

996. **Cutaneous Vasodilatation during Fainting**
E. S. SNELL, W. I. CRANSTON, and J. GERBRANDY. *Lancet* [*Lancet*] **1**, 693–695, April 2, 1955. 4 figs., 15 refs.

The authors, from St. Mary's Hospital Medical School, London, report observations on changes in body temperature, pulse rate, blood pressure, and elimination of heat from the hand recorded during 9 fainting fits among 6 subjects. Body temperature was measured by thermocouples inserted sublingually and rectally, and heat elimination by means of a calorimeter. Three of the faints observed were provoked in a healthy woman student by venepuncture and withdrawal of 5 ml. of blood, and the remaining 6 faints occurred in 5 men after the intravenous injection of 16 to 200 ml. of the subjects' own blood containing bacterial pyrogens. Two of the latter occurred during the onset of fever, and 4 within 10 minutes of the injection and at least 45 minutes before the onset of fever.

There was an increase in heat elimination from the hand during all the faints, with a simultaneous fall in blood pressure and transient bradycardia. Changes in body temperature were variable.

Comparing these observations with the effects of intravenous injection of pyrogens in blood in 40 other experiments where fainting did not ensue, the authors conclude that the faints were mostly emotional in origin. The changes in heat elimination from the hand are interpreted as indicating cutaneous vasodilatation.

H. F. Reichenfeld

997. **Subcutaneous Cords on the Trunk.** [In English]
G. JÖNSSON, F. LINELL, and P. SANDBLOM. *Acta chirurgica Scandinavica* [*Acta chir. scand.*] **108**, 351–367, 1955. 13 figs., 27 refs.

A description is given of 8 cases, observed at the University Hospital, Lund, Sweden, of the condition often known as "Mondor's disease" (although it was described by several authors before Mondor). The condition is characterized by the presence of firm, cord-like, subcutaneous indurations, most common on the trunk. They are palpable and can be made conspicuous by stretching the skin. while attachment of a cord to the skin may cause the latter to retract.

Microscopically, the cords are largely composed of longitudinal collagen fibres, but in one of the authors' cases sections from different parts of a cord showed all stages of transition from a vascular structure with perivascular fibrosis to a solid cord of connective tissue. It has previously been assumed that the cords are derived in some way from veins, but the present authors show that they probably originate from lymph trunks and that the condition follows a lymphangitis. No treatment is required and in course of time the cords disappear spontaneously.

D. M. Pryce

DIAGNOSTIC METHODS

998. **The Electrocardiogram in Primary Endocardial Fibroelastosis**
P. VLAD, R. D. ROWE, and J. D. KEITH. *British Heart Journal* [*Brit. Heart J.*] **17**, 189–197, April, 1955. 6 figs., 38 refs.

An analysis is presented from the University of Toronto of electrocardiograms (ECGs) recorded from standard, unipolar, and precordial leads in 23 cases of primary endocardial fibroelastosis proven at necropsy. Ten of these have been reported in the literature by various authors; the remainder were new cases observed at hospitals in Toronto, Montreal, and New York.

Electrical changes due to left ventricular enlargement or thickening were recorded in 16 cases. Signs of right ventricular hypertrophy were recorded in 7 cases—either in a pure form (4 cases) or in the form of combined ventricular hypertrophy (3 cases); only in one of the former, however, did subsequent tracings fail to show some left ventricular hypertrophy. In 14 cases there were alterations of the P wave indicating hypertrophy or dilatation of one or both atria.

These findings indicate that endocardial fibroelastosis need not necessarily be excluded from the differential diagnosis merely because of lack of evidence of left ventricular strain in the ECG. It is noted that in all the patients with marked right ventricular hypertrophy the disease either ran a chronic course or was atypical anatomically. On the other hand in fulminating cases the tracings did not show any evidence of right ventricular hypertrophy.

In cases of enlargement of the heart in infancy unaccompanied by central cyanosis, murmurs, or shunts the ECG may be of crucial importance in differentiating between endocardial fibroelastosis, interstitial myocarditis, glycogen disease of the heart, and anomalous origin of the left coronary artery from the pulmonary artery. The characteristic findings in these conditions are discussed.

William A. R. Thomson

999. **The Intracardiac Electrogram as an Aid in Cardiac Catheterization**
D. EMSLIE-SMITH. *British Heart Journal* [*Brit. Heart J.*] **17**, 219–224, April, 1955. 10 figs., 16 refs.

Electrocardiograms have been recorded by the author through unipolar leads from the great veins and cavities of the right heart during catheterization in 30 cases of congenital or rheumatic heart disease out of a series of 130 such cases studied at the Royal Infirmary, Dundee (University of St. Andrews). The technique is described as "a simple addition to routine cardiac catheterization; it is neither expensive nor time-consuming". It is claimed that location of the catheter tip by watching the intracardiac electrogram throughout the procedure lessens

the risk in cardiac catheterization by reducing screening time to a minimum and enabling trauma to the endocardium and accidental catheterization of the coronary sinus to be avoided. In addition, it is of value in the interpretation of pressure tracings; for instance, " the shape of the electrogram will often permanently identify the site of a pressure pulse or a blood sample ", while " injury currents provide a means of recognizing that unexpectedly low pressure pulses are the result of partial occlusion of the catheter by endocardium, and are consequently invalid ". *William A. R. Thomson*

1000. **The Electrocardiographic Spatial Magnitude Curve in Man**

B. M. SAYERS, F. G. SILBERBERG, and D. F. DURIE. *American Heart Journal* [*Amer. Heart J.*] **49**, 323–335, March, 1955. 5 figs., 9 refs.

The authors describe a study carried out at the Alfred Hospital, Melbourne, of the magnitude of the spatial vector in the electrocardiogram, based upon the hypothesis that the human heart may be considered to act as a small electric dipole in a poorly conducting medium which is believed to be largely homogeneous. The magnitude–time curve of the spatial electrocardiogram is defined as the time curve of the magnitude of the spatial vector representing the manifest cardiac dipole without reference to direction. In an analysis of the records obtained from 95 patients it was shown that all the tracings studied fell into a continuously graded two-dimensional sequence, many different types of cardiac abnormality showing curves scattered throughout the sequences. All the cases of left bundle-branch block showed a similar type of curve, which differed from that produced by left ventricular hypertrophy. Evidence is presented which suggests that high-frequency components of the spatial magnitude vector electrocardiogram may be of considerable significance.

William A. R. Thomson

CONGENITAL HEART DISEASE

1001. **The Technique and Complications of Pulmonary Valvotomy with Special Reference to the Transarterial Approach**

F. THERKELSEN. *Thorax* [*Thorax*] **10**, 19–22, March, 1955. 6 figs., 4 refs.

The author describes his experience of valvotomy in 63 cases of pulmonary stenosis at Rigshospitalet, Copenhagen. He considers valvotomy to be indicated in all such cases provided the stenosis is of valvular type—whether it (1) occurs as an isolated lesion or in association with atrial septal defect, or (2) forms part of the tetralogy of Fallot; in the series reported, 31 cases belonged to the first group and 32 to the second. Three types of operation were performed: in 34 cases a transventricular approach was employed, in 11 cases a transarterial approach with the use of a special clamp, and in the remaining 18 cases a " direct " transarterial technique. This last operation, which involves the use of special instruments for cutting the valve, is described, and reasons are given for considering it superior to the other methods used.

There were 4 deaths in the series—3 in cases in which the transventricular approach was used and one following a transarterial operation.

[No figures of late results are given in comparison with those of other methods of approach to the pulmonary valve.] *J. R. Belcher*

1002. **Surgical Treatment of Forty-six Interatrial Septal Defects by Atrio-septopexy**

C. P. BAILEY, H. T. NICHOLS, H. E. BOLTON, W. L. JAMISON, and H. GOMEZ-ALMEIDA. *Annals of Surgery* [*Ann. Surg.*] **140**, 805–820, Dec., 1954. 14 figs., 20 refs.

The operation of atrio-septopexy as originally devised consisted in closing an atrial septal defect by suturing an invaginated portion of the right atrial wall to the margins of the defect. Increasing experience has shown, however, that if the defect is large there may not be a complete rim of septal tissue and complete closure by this method may not be possible. Recently the authors have come to the conclusion that closure is not necessary so long as the systemic and pulmonary venous systems can be separated. In some cases this problem has been solved by suturing the atrial wall to the free edge of the posterior septal remnant, thus converting the right atrial cavity into a U-shaped chamber lying behind the defect. (This modification has been named the " Pompeian version " of atrio-septopexy, by analogy to the ancient Pompeian method of manufacturing water-pipes.) The modified operation is very satisfactory in patients with a persistent remnant of lower septal tissue, but is not so suitable when the septum primum is totally absent, whether or not a septum secundum is present. Attempts to apply the technique in such cases may lead to damage to the bundle of His as it runs along the free upper margin of the muscular part of the interventricular septum. In these cases it is safe to complete the intracardial channel except for a short interval between the upper lip of the ostium of the coronary sinus and the most anterior (membranous) portion of the interventricular septum; the residual gap may then be closed with a small bag of pericardial fat placed on the left atrial side of the defect after carrying out Kiriluk's technique.

Anomalous pulmonary venous return may be dealt with at the same operation. If only one vein empties abnormally it may be re-implanted into the side of the normally emptying vein. However, if both right pulmonary veins drain into the right atrium they may be excluded by suturing the lateral atrial wall to the anterior margin of the septal defect, thus converting the right atrium into two compartments, of which the small posterior one drains the right pulmonary veins directly into the left atrium. Co-existent mitral stenosis can be dealt with at the same time through the right atrial appendix and the atrial septal defect.

At Hahnemann Medical College Hospital, Philadelphia, these operations have been performed after intravenous injection of procaine and under thiopentone anaesthesia with endotracheal oxygen. With the patient supine the chest is opened in the 4th intercostal space, the costal cartilages being divided at the sternum. The

ungloved left index finger is used to palpate the interior of the heart and the findings are confirmed by means of a Bolton cardioscope. The authors believe that the closed technique is better than an open method at the present time, and that hypothermia gives no added advantage, especially in adults. A total of 46 patients have so far been operated on. Among 30 patients with septum secundum atrial defects there were 3 operative deaths, but all the survivors showed marked clinical improvement, with complete abolition of the shunt in the majority. Among the 16 patients with ostium primum septal defects there were 11 operative deaths, 3 due to heart block, 2 to congestive failure, one from the effects of an aortico-atrial fistula produced at operation, one from inadequate closure of the defect, one from the results of a technical error by which the inferior vena cava was shunted into the left atrium, 2 from mitral insufficiency due to distortion of the valve, and one from failure to recover from the effects of hypothermia.

In conclusion the authors state their belief that correction of an interatrial communication is not indicated in patients with a right-to-left shunt, since in them the defect has come to have a partially compensatory function. They urge that these patients be diagnosed and treated in early childhood, before irreversible myocardial damage, pulmonary vascular changes, or impairment of physical development have developed. The optimum time for treatment, on both surgical and physiological grounds, is between the ages of 4 and 6 years.

[This important paper should be read by all cardiac surgeons.] *F. J. Sambrook Gowar*

1003. Patent Ductus Arteriosus with Pulmonary Hypertension

W. WHITAKER, D. HEATH, and J. W. BROWN. *British Heart Journal* [*Brit. Heart J.*] **17**, 121–137, April, 1955. 14 figs., 12 refs.

The association of severe pulmonary hypertension with patent ductus arteriosus in 8 cases is descrioed in this paper from the City General and Royal Hospitals, Sheffield. Dyspnoea, cyanosis, recurrent chest infections, and haemoptysis were the leading symptoms, while the signs were those of pulmonary hypertension—namely, a systolic lift over the right ventricular outflow, palpable pulmonary valve closure with a loud pulmonary second sound, and giant " a " waves in the jugular pulse. The signs of patent ductus arteriosus were inconspicuous: a Gibson murmur was present in one case only; 3 patients had no murmurs, 2 had a basal systolic murmur, and 2 had a basal diastolic murmur. The electrocardiogram showed right ventricular predominance or right bundle-branch block in all cases. Chest radiographs showed prominence of the pulmonary artery and its branches in varying degree.

In 2 cases the diagnosis was confirmed at necropsy. Cardiac catheterization was carried out on the remaining 6 patients, in all of whom arterial systolic pressure was 100 mm. Hg or more. In 5 of the 6 the catheter was passed through the ductus into the descending aorta. Angiocardiograms showed simultaneous filling of the pulmonary arteries and descending aorta. Associated lesions were found in 3 cases—an overriding aorta, a ventricular septal defect, and mitral stenosis respectively.

The authors consider that the possibility of patent ductus arteriosus should be considered in the differential diagnosis in all cases with clinical evidence of pulmonary hypertension. *C. W. C. Bain*

DISTURBANCES OF RHYTHM AND CONDUCTION

1004. The Nature of Spontaneous Auricular Fibrillation in Man. With Comments on the Action of Antiarrhythmic Drugs

M. PRINZMETAL, L. RAKITA, J. L. BORDUAS, E. FLAMM, and A. GOLDMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1175–1182, April 2, 1955. 7 figs.

The exact mechanism of auricular fibrillation in man has never been satisfactorily demonstrated. As a contribution to this subject the authors took the opportunity during the surgical treatment of patients with mitral stenosis and auricular fibrillation at the Cedars of Lebanon Hospital, Los Angeles, to obtain direct electrocardiograms from the fibrillating auricles and also to make high-speed cinematographic records.

By neither method was any evidence adduced for the " circus movement " postulated by Lewis. The electrocardiograms showed large waves occurring irregularly at a rate of 250 to 400 per minute, with in addition highly irregular small waves along the base line. It has been shown previously that auricular flutter is due to the presence in the auricle of a rapidly discharging ectopic focus, and that auricular tachycardia, auricular extrasystoles, and auricular flutter are essentially of the same nature, in that the contraction pursues an orderly course from the site of origin to the extremities of the auricles. It is argued that if the rate of contraction of the ectopic focus exceeds a critical threshold—which varies in different patients—there is a complete breakdown of orderly mechanical and electrical activity, and auricular fibrillation results. This has been experimentally demonstrated on the heart of the dog.

The application of these findings to treatment is considered, and in a discussion of the action of drugs it is suggested that if the action of quinidine is gradually to slow the rate of discharge from an ectopic focus all the effects of this drug in varying doses can readily be explained. It is considered probable that procainamide acts similarly. *C. Bruce Perry*

1005. A–V Block and Cardiac Output

J. H. BURN, E. M. V. WILLIAMS, and J. M. WALKER. *British Medical Journal* [*Brit. med. J.*] **1**, 574–576, March 5, 1955. 2 figs., 1 ref.

The authors describe experiments carried out at the University of Oxford in which the Starling heart–lung preparation of the dog was used to determine the cardiac output during electrical stimulation of the right auricle. They show that as the rate of stimulation was increased the ventricular rate also increased and the cardiac output

fell—in three of the experiments to zero. With the spontaneous onset of A–V block the output increased, and usually reached its greatest value when the block was in the ratio of 3:2. When the ratio changed to 2:1 cardiac output fell, but this lower output was well maintained throughout the period after the block began. In experiments in which acetylcholine was infused into the preparation electrical stimulation of the auricle led to auricular fibrillation, the onset of fibrillation coinciding with a rise in cardiac output. From these observations the authors conclude that A–V block and auricular fibrillation are mechanisms whereby the ventricular rate is controlled and the cardiac output maintained.

A. I. Suchett-Kaye

1006. **Upper Atrio-ventricular Nodal Beats Precipitated by Ventricular Extrasystoles with Retrograde Conduction**
A. SCHOTT. *British Heart Journal* [*Brit. Heart J.*] **17**, 247–254, April, 1955. 4 figs., 14 refs.

An unusual ectopic arrhythmia is described which showed ventricular extrasystoles with systematically increasing and at other times systematically decreasing coupling. Extrasystoles falling comparatively early in diastole showed signs of retrograde conduction to the auricles and only these were followed by upper A-V nodal post-extrasystolic beats. In a second case the post-extrasystolic intervals after ventricular extrasystoles with retrograde conduction to the auricles were also terminated by upper A-V nodal beats. Reasons are given for the view that the variations in coupling were due to disturbances in impulse formation and not to disturbances in impulse conduction. Facilitation of conduction in the auricles of the A-V nodal post-extrasystolic beats is put forward as a tentative explanation for the occurrence of A-V nodal escape beats and temporary post-extrasystolic A-V nodal rhythm with preceding activation of the auricles.—[Author's summary.]

1007. **Mitral Incompetence in Experimental Auricular Fibrillation**
R. DALEY, I. K. R. MCMILLAN, and R. GORLIN. *Lancet* [*Lancet*] **2**, 18–20, July 2, 1955. 4 figs., 3 refs.

PERICARDITIS

1008. **The Early Diastolic Sound of Constrictive Pericarditis**
P. MOUNSEY. *British Heart Journal* [*Brit. Heart J.*] **17**, 143–152, April, 1955. 8 figs., 13 refs.

In 18 out of 22 patients with constrictive pericarditis examined at the London Hospital an early diastolic sound, as originally described by Potain in 1856, was heard and recorded phonocardiographically. This sound, heard widely over the praecordium, was loud and snapping and was often accompanied by a palpable diastolic thrust. It usually occurred slightly later in the cycle than the opening snap of mitral stenosis, and decidedly earlier than a normal third sound. After the successful performance of pericardiolysis the sound changed so as to resemble a third sound both in time and in character.

Simultaneous recording of the phonocardiogram and the pressure in the right heart in 4 cases showed that the early diastolic sound coincided with a steep upstroke in the pressure recording following an early diastolic dip, signifying an abrupt check in the rapid filling of the right ventricle. It is suggested that the rapid filling is due to the raised jugular pressure in these cases, and the abrupt check to the ensheathing pericardium; the changes in character and timing of the sound are those which would be expected to result from the fall in venous pressure and the removal of the pericardial casing. In 2 cases in which the sound was not present the upstroke in the pressure recording was less steep, suggesting a less abrupt check and a slower filling of the ventricle.

An experiment is described in which abrupt halting of rapid ventricular filling was simulated in a model by allowing water from a reservoir to enter a collapsible but non-distensible rubber tube. Pressure and sound recordings from the rubber tube resembled " in broad essentials " the findings in constrictive pericarditis, providing support for the author's theory concerning the mechanism of production of the early diastolic sound in constrictive pericarditis.

C. W. C. Bain

1009. **Results of Radical Pericardiectomy for Constrictive Pericarditis**
E. HOLMAN and F. WILLETT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 789–794, March 5, 1955. 7 figs., 5 refs.

In reporting their experience of the treatment of constrictive pericarditis the authors stress the need for more radical surgery in this condition, regarding delay in improvement and need for a second operation as due to inadequate pericardiectomy. They consider that when calcification is present, even if symptoms are mild, decortication should be performed, as cardiac disability is progressive. In tuberculous pericarditis decompression of the heart by aspiration or operation is indicated as soon as symptoms of compression appear. The operation they use is as follows. The pericardium is excised to beyond the left, right, and the inferior borders of the heart, and often over the venae cavae at the base. A mid-line incision is made, with vertical division of the sternum, which is repaired with at least three steel stitches over which the pectoral fascia is reapproximated. The decortication is begun over the apex and the left side liberated first, excising through a plane just outside the muscle, sometimes in two layers. If the heart is irritable and becomes irregular there should be a few moments' delay. Haemorrhage from the heart can be controlled by stitching down a small flap of the mobilized pericardium. The mediastinum and the right pleural cavity are drained. Full chemotherapy is given before and after operation.

The authors have performed this operation on 26 patients with constrictive pericarditis, the oldest aged 55. There were no operative deaths, but 4 patients died subsequently, 2 from myocardial failure and 2 from unrelated causes. The other 22 patients—8 with tuberculous and 14 with non-tuberculous pericarditis—are all well, although 3 in each group have some limitation of activity.

Venous pressure was consistently reduced immediately after operation, and in some cases there was also marked improvement in arterial pressure. The pericardium was usually thickest in its right lower part, with intimate involvement of the diaphragm, and the authors suggest that this may account for the paradoxical pulse, as it prevents cardiac contraction during inspiration.

M. Meredith Brown

ENDOCARDITIS

1010. **Four Years' Observation following Splenectomy for Osler's Disease (Subacute Bacterial Endocarditis).** (Quatre ans d'observation de la splénectomie dans la maladie d'Osler)

G. GIRAUD, P. CAZAL, H. LATOUR, A. LÉVY, P. PUECH, and M. RIBSTEIN. *Montpellier médical* [*Montpellier méd.*] 46, 552–559, Dec., 1954.

In reporting 3 cases of subacute bacterial endocarditis in which splenectomy gave good results the authors distinguish 3 types of change which may occur in the spleen in this disease: (1) septic emboli; (2) arteriolar changes, probably arising from infarction due to the organization of toxic substances liberated under the influence of antibiotic treatment; and (3) residual fibrous changes in the reticulo-endothelial system. Theoretically, they consider it possible that some instances of "relapse" in subacute bacterial endocarditis may be due, not to a flare-up of the infective process, but to a general tissue reaction of an allergic nature.

The following indications for splenectomy are given: (1) major splenic infarct or abscess (when splenectomy is considered a matter of urgency); (2) cases where antibiotic treatment is only partially effective or resulting improvement is not maintained and where (*a*) there is splenomegaly with periods of pyrexia frequently accompanied by increase in size of the spleen or fluctuations in the erythrocyte sedimentation rate (E.S.R.), particularly if splenic puncture reveals streptococci, or (*b*) despite the absence of pyrexia the spleen remains consistently enlarged and a raised E.S.R. persists or recurs.

A. Schott

1011. **Staphylococcal Endocarditis. Some Clinical and Therapeutic Observations on Thirty-eight Cases**

A. M. FISHER, H. N. WAGNER, and R. S. ROSS. *Archives of Internal Medicine* [*Arch. intern. Med.*] 95, 427–437, March, 1955. 16 refs.

The authors describe the results of treatment in 38 cases of staphylococcal endocarditis at Johns Hopkins Hospital, Baltimore. These fell into 3 groups: (I) 22 cases treated before antibiotics became available; (II) 3 cases treated between 1944 and 1948, when effective doses of penicillin were used and most strains of staphylococci were sensitive to the drug; and (III) 13 cases treated in the period 1949–53. Of the total number, the pre-existing heart disease was congenital in 10, rheumatic in 9, and hypertensive–arteriosclerotic in 6; in 13 there was no pre-existing cardiac condition. All but one of the 22 patients in Group I died, treatment in the successful case being with sulphanilamide, antiserum, and blood transfusion; in Group II there were 2 deaths and one recovery; while in Group III 6 patients survived and 7 died.

The authors discuss problems in diagnosis and treatment, mostly on the basis of the 13 cases in Group III, and illustrate these with a number of case reports, among them one of rheumatic mitral and aortic valvular disease in which blood cultures were positive for *Staphylococcus aureus* but no evidence of bacterial endocarditis was found at necropsy. Among difficulties in diagnosis are mentioned the mildness of the condition when first seen and the finding of a normal leucocyte count. In one case cortisone given for a coexistent condition was considered to be a factor in the failure of treatment of the bacterial endocarditis.

The bactericidal and bacteriostatic effect of the patient's serum in different dilutions against the infecting staphylococcus is considered to be a useful guide to therapy. For testing the sensitivity of the staphylococcus to various antibiotics as well as to penicillin the tube dilution test was found to be more satisfactory than the disk method.

The authors conclude that in cases of bacterial endocarditis, even when there are indications that the organism is resistant to the drug, penicillin should always be given in doses ranging from 8 to 24 mega units a day. Erythromycin in large doses—up to 3·6 g. a day for 5 weeks—may also be given, with one of the broad-spectrum antibiotics in addition. As regards length of treatment, the authors state that they "would hesitate . . . to advocate stopping [treatment] any sooner" than the 6th or 7th week.

G. S. Crockett

CORONARY DISEASE

1012. **Clinical Evaluation of Biphosphate of Triethanolamine Trinitrate in Coronary Insufficiency.** (Evaluacion clínica del bifosfato de trinitrato de trietanolamina en la insuficiencia coronaria)

T. CESARMAN and D. CAZÉS. *Archivos del Instituto de cardiología de México* [*Arch. Inst. Cardiol. Méx.*] 24, 514–522, Sept.–Oct., 1954 [received March, 1955]. 11 refs.

The effect of triethanolamine trinitrate on 33 patients (31 males, 2 females) ranging in age from 42 to 69 with angina pectoris due to coronary disease was studied. In some of the cases the initial dose was 3 to 6 mg. a day, which was increased up to 12 mg. when necessary. In others it was 10 to 12 mg., which was gradually reduced. With one exception, treatment lasted between one and 8 months.

The results were considered "excellent" in 14 (43%) and "good" in 8 cases (24%). In the remaining 11 (33%) no effect was seen. No side-effects were observed. In 10 cases other drugs were given or tobacco withheld which, as the authors admit, might have influenced the results of this trial. No control tests with a placebo were carried out.

[At one point it is stated that one patient also had a diaphragmatic hernia; from a subsequent passage it would appear that there were 3 patients with this condition.]

A. Schott

1013. **An Evaluation of the Effect of Choline and Inositol on the Clinical Course and Serum Lipids in Patients with Angina Pectoris**

R. S. JACKSON, C. F. WILKINSON, L. MEYERS, M. S. BRUNO, and M. R. BENJAMIN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 583–594, March, 1955. 6 refs.

In order to test the effect of lipotropic agents on atherosclerosis a controlled experiment was carried out at Bellevue Hospital (New York University), New York, on 40 patients with angina pectoris. The "double-blind" technique was used, the experiment lasting for a period of 12 months during one-half of which the patient took about 9 g. of choline and about 1·4 g. of inositol daily in a syrup (the exact amount being determined by weighing the medicine remaining at each visit), and during the other 6 months a placebo syrup without the lipotropic factors, the order in which the two preparations were given to each patient being determined at random. During the whole 12 months the only other drugs allowed were nitroglycerin tablets, and the number of these used and the amount of pain suffered were recorded daily by the patient on a special card. This card was checked at each visit to the clinic, and at the same time heparinized blood was taken for the determination of plasma cholesterol and lipid phosphorus levels. The usual interval between visits was 3 weeks.

The results were subjected to rigid statistical analysis. No significant clinical improvement or reduction in the requirement of nitroglycerin tablets could be detected during either period. The mean plasma cholesterol and phospholipid levels were significantly higher (by about 20 to 30 mg. per 100 ml.) during choline–inositol treatment, but the fluctuation of these levels in individual patients was not significantly influenced by the administration of the lipotropic factors.

[These findings are in accordance with those of Duff and Meissner (*Arch. Path.* (*Chicago*), 1955, **57**, 329) and of Wissler *et al.* (ibid., p. 333), who found that choline seemed to have no preventive effect against the lesions of experimental atherosclerosis in rabbits and in rats respectively.] *Z. A. Leitner*

HYPERTENSION

1014. **Late Systemic Complications of Hydralazine (Apresoline) Therapy**

J. C. MULLER, C. L. RAST, W. W. PRYOR, and E. S. ORGAIN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 894–899, March 12, 1955. 3 figs., 18 refs.

A description is given of a collagen-like illness ("hydrallazine reaction") which developed in 7 of 53 hypertensive patients given hexamethonium chloride and hydrallazine ("apresoline") simultaneously for periods of 4 to 23 months at Duke Hospital, Durham, N. Carolina. These 7 patients had received an average maximum daily dosage of 475 mg. of hydrallazine for a minimum period of 6 months. All complained of aching, stiffness, and soreness of joints; in addition there was periarticular swelling of the proximal interphalangeal joints in 4 cases, with hot, painful swellings of the knees and ankles in 2 and effusion in one. Other symptoms included fever, sore throat, chilly sensations, pleuritic chest pain, and malaise. In one case the illness resembled acute systemic lupus erythematosus, with fever, arthritis, pericarditis, pleural effusion, and the presence of L.E. cells. This condition subsided after hydrallazine was stopped and treatment with ACTH and cortisone instituted. L.E. cells were discovered in 2 of the 5 affected patients on whom laboratory studies were performed; they were also found in 2 asymptomatic patients during treatment with hydrallazine. Bone-marrow function was depressed in some cases, but recovered on withdrawal of the drug.

The authors consider that, in view of these reactions, hydrallazine should be reserved for patients with severe hypertensive states in which morbidity and mortality overshadow potential dangers associated with the effects of the drug itself. *I. Ansell*

1015. **Long-term Management of Hypertension with Pentolinium Tartrate (Ansolysen)**

A. AGREST and S. W. HOOBLER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 999–1003, March 19, 1955. 2 figs., 7 refs.

The authors report their experience with pentolinium tartrate ("ansolysen") in the treatment of 31 cases of hypertension at University Hospital, Ann Arbor, Michigan. The series was composed of 19 males and 12 females ranging in age from 33 to 58 years. In 23 cases one or more complications—including coronary thrombosis, congestive cardiac failure, retinopathy, uraemia, or transient cerebrovascular episodes—had developed, and in the remaining 8 the diastolic pressure had consistently exceeded 120 mm. Hg. Ten of the 31 patients had previously undergone supradiaphragmatic sympathectomy.

To determine the dosage of ansolysen needed by each patient an initial dose of 20 mg. was given at 8 a.m., 3 p.m., and 10 p.m., and was increased by 20 mg. each day until the lowest systolic pressure recorded in the standing position at various times during the day was 110 to 130 mm. Hg. This point was usually reached during the afternoon. After discharge the patient returned at intervals for the dosage to be checked in relation to the systolic pressure. In some patients the systolic pressure could be reduced to 90 to 100 mm. Hg without giving rise to undue side-effects. To counteract the tendency to irregular absorption associated with constipation a daily laxative in the form of magnesia or cascara was prescribed. Reserpine ("serpasil"), 0·25 mg. 3 times daily, was given in addition to ansolysen in 15 cases. Hydrallazine ("apresoline") was also tried in a few cases, but without noticeable additive effect.

In all the 9 cases in which congestive cardiac failure was a complication this was controlled. Of the 7 patients who had had cerebrovascular episodes, 6 were free from further attacks for an average of 4·8 months, the remaining patient dying of a cerebral haemorrhage during treatment. Three of the 5 patients with uraemia died,

but in 3 out of 4 cases of disabling retinopathy there was some symptomatic improvement.

The " mean standing blood pressure " (defined as one-half the sum of systolic and diastolic pressures recorded at half-hourly intervals with the patient standing) was reduced by 20 mm. Hg or more in 87% of patients, returning to normal in 31%. With the patient recumbent a reduction of more than 20 mm. Hg resulted in 68%, but a return to normal was obtained in only one patient. In 4 cases no significant reduction in blood pressure was observed.

Side-effects, consisting in blurring of vision, constipation, and orthostatic hypotension, were noted in all cases, in 24 of them making a reduction in the dose necessary, while in one case treatment had to be discontinued.

[That these patients were observed for only one to 9 months from the beginning of treatment hardly justifies the use of " long-term " in the title of this paper.]

H. F. Reichenfeld

1016. **Oral Preparations of *Rauwolfia serpentina* in Treatment of Essential Hypertension**

S. LOCKET. *British Medical Journal* [*Brit. med. J.*] 1, 809–813, April 2, 1955. 2 figs., 14 refs.

At Oldchurch Hospital, Romford, Essex, the author has treated 39 severely hypertensive patients with preparations of *Rauwolfia serpentina*. All of them were fully ambulatory out-patients, and the period of treatment ranged from 6 to 20 months. Two preparations of rauwolfia were used, one of total root extract which was given in a dose of 500 or 1,000 mg. daily, and one of total active alkaloids (" rauwiloid "), given in doses of 4 or 8 mg. daily. Inert tablets were substituted for the active drugs during part of the course.

The effect of treatment on the level of the diastolic blood pressure was as follows. There was no reduction in 16 cases, a slight but consistent fall of 10 to 20 mm. Hg in 7 cases, an appreciable fall, greater than 20 mm. Hg but not reducing the pressure below 100 mm. Hg, in 12 cases, while the pressure was consistently reduced to below 100 mm. Hg in 4 cases.

The pressure rose again when administration of the drug was stopped. Precipitate falls in blood pressure and postural hypotension did not occur, but side-effects were common. Mental depression occurred in 5 patients, necessitating withdrawal of treatment in 2, one of whom had attempted suicide. Two other patients had to stop treatment because of diarrhoea, and 6 other patients also suffered from diarrhoea. Other side-effects complained of included lack of energy, nasal congestion, nausea and vomiting, loss of libido, and amaurosis. On the other hand symptoms complained of before treatment were very often relieved, though such relief was obtained equally with the inert tablets. The preparation seemed to be more effective in male and in elderly arteriosclerotic patients, but it was ineffective when papilloedema was present. The author states that these preparations of rauwolfia are the most effective and useful orally administered agents he has yet used in the treatment of essential hypertension, and he considers them fully worthy of a further trial.

[It seems surprising that the author should have arrived at this conclusion on the basis of the findings reported. Only 4 of his patients achieved a fall in diastolic blood pressure which might be considered likely to be of real clinical value, while 5 developed mental depression and other side-effects were common. Moreover, 80% of his patients seemed to obtain relief of symptoms while taking only a placebo.]

Bernard Isaacs

1017. **Reserpine in Hypertension**

I. SINGH. *British Medical Journal* [*Brit. med. J.*] 1, 813–817, April 2, 1955. 5 refs.

The author has treated 33 hypertensive patients with " serpasil " (reserpine). Apart from 2 with malignant hypertension, all the patients were ambulant and were treated as out-patients. The dose of reserpine was 0·25 mg. thrice daily when the systolic blood pressure was initially below 200 mm. Hg, and 0·5 mg. thrice daily when it was above that level.

In most of the early and mild cases of essential hypertension the blood pressure fell to normal within a few days of starting treatment, and remained normal when the dose was reduced to maintenance level. In few of the patients with malignant hypertension, renal hypertension, or benign essential hypertension of considerable duration or severity, however, was any significant fall of blood pressure obtained. Side-effects were frequent but not very troublesome, and usually passed off in time. Bradycardia was a consistent finding and was unrelated in degree to the fall in blood pressure. Both the blood pressure and the pulse rate rose after muscular exercise in patients receiving reserpine; one patient with malignant hypertension developed a myocardial infarction during treatment. The author considers that reserpine is useful in the treatment of all types of hypertension, as even when no direct response is obtained, as in severe and chronic cases, use of the drug facilitates later treatment with hexamethonium.

Bernard Isaacs

1018. **The Treatment of Essential Hypertension with Pentolinium Tartrate Combined with Rauwolfia Alkaloids**

C. W. C. BAIN, F. ASHTON, and B. P. JONES. *British Medical Journal* [*Brit. med. J.*] 1, 817–818, April 2, 1955. 3 refs.

A report is presented on the treatment at Harrogate General Hospital of 17 patients suffering from severe essential hypertension without renal involvement. Under treatment with pentolinium tartrate alone the blood pressure was " stabilized " at a satisfactory level in most cases, but disturbing side-effects were consistently present, the mean daily dose of pentolinium required being 840 mg. Rauwolfia alkaloids (in the form of " rauwiloid ") in a single daily dose of 4 mg. were then added, when the mean daily dose of pentolinium required to maintain stabilization fell to 240 mg. and there was a striking decrease in the incidence of undesirable side-effects. It is now the authors' practice, when initiating the drug treatment of hypertension, to give rauwolfia alone for some weeks and to add pentolinium thereafter.

Bernard Isaacs

1019. **The Relations between Renal Blood Flow, Arterial Blood Pressure, and Retinal Lesions in Nephritis and Essential Hypertension.** (Existe-t-il une corrélation entre le flux sanguin rénal, la tension artérielle et les lésions rétiniennes chez les néphritiques et les hypertendus essentiels?)

F. Reubi, G. Novak, and R. Witmer. *Helvetica medica acta* [*Helv. med. Acta*] **22**, 1–15, Feb., 1955. 9 figs., 14 refs.

The authors have investigated, at the University Medical and Ophthalmological Clinics, Berne, the relationship, if any, between renal blood flow, arterial blood pressure, and retinal lesions in 80 cases of essential hypertension with or without nephrosclerosis, 21 of acute glomerulonephritis, and 28 of chronic glomerulonephritis. Renal plasma flow was estimated on 243 occasions by determining the clearance of sodium PAH. In 37 cases, however, the severity of the renal lesions rendered doubtful the validity of this method as a measure of renal plasma flow, and in these the extraction rate was determined by venous catheterization and a correction factor applied. A total of 256 ophthalmic examinations were made, when possible on the same day as the clearance estimations. Retinal changes were graded into the usual four stages; 178 measurements were also made of the diastolic pressure in the retinal vessels, this value divided by the systemic diastolic pressure giving the index of Bailliart.

In the cases of essential hypertension there was a rough correlation between the retinal changes and renal plasma flow, but there were numerous exceptions and a notably wide range of variation. There was no correlation between renal plasma flow and retinal arterial pressure or the index of Bailliart, but there was a direct correlation between the mean blood pressure and the degree of retinal change. The renal blood flow was generally reduced if the blood pressure was raised, but not proportionately.

The cases of chronic glomerulonephritis also showed a direct correlation between the rise in blood pressure and the extent of the retinal changes, but no correlation between retinal tension and renal blood flow. There was also a close relationship between renal blood flow and either retinal changes or increase in blood pressure, but in most cases hypertension did not appear until the renal plasma flow was below 300 ml. per minute. The majority of the patients with acute glomerulonephritis showed no alteration in the retinal vessels or in the renal plasma flow, even though some of them also had hypertension. The index of Bailliart was nearly always elevated, suggesting that there was some peripheral retinal vasoconstriction, although evidence of this was not demonstrable.

The authors conclude that retinal changes are of prognostic value if severe, but they do not help to differentiate cases of essential hypertension from those of chronic glomerulonephritis. They suggest that the absence of retinal changes in cases of hypertensive renal disease is suggestive of acute nephritis. In their experience a reduction of renal plasma flow in patients with acute nephritis indicates a bad prognosis.

D. Goldman

PERIPHERAL ARTERIES

1020. **Clinical Investigation by the Oscillogram of Peripheral Arteries**

M. G. Kettner, C. Ferrero, and P. W. Duchosal. *American Heart Journal* [*Amer. Heart J.*] **49**, 485–500, April, 1955. 14 figs., 8 refs.

An analysis of the oscillograms (tracings of arterial oscillations) of the extremities of 127 subjects, both normal and diseased, is presented. Tracings were made with a specially constructed differential manometer based on the principle of the torsion–tension relationship of a twisted metal band, and utilizing an ordinary blood pressure cuff. An accurate standardization of the recordings was effected by use of a hypodermic syringe in the pneumatic system. Nitroglycerin was given as a test for vasodilatation. Records were taken with cuff pressure below the level of diastole, before and after medication.

A consistent pattern was seen in the ankle oscillograms in the fifty-eight normal subjects studied. The patterns of tracings taken from the fingers and forearms were inconsistent and variable. Of forty-four patients with arterial disease, twenty-seven showed abnormally shaped pulse forms in ankle oscillograms. The remainder showed normally or equivocally shaped forms. A number of the twenty-five patients with various other diseases showed different degrees of abnormality, although most showed normal tracings. No absolute criteria as to timing and size of pulsations, or response to nitroglycerin, could be established, since there was a great overlap between the normal and diseased groups. A brief discussion of the principles involved is presented. Although more accurate than the clinical determination of the oscillometric index, the oscillogram as recorded by this method is still of limited clinical value. The method promises to be of value in investigative work, by providing an objective measurement of the clinical evaluation of disease states of peripheral arteries, the effects of drugs, and the results of treatment. The manometer described may also be useful in other physiological and clinical studies.—[Authors' summary.]

1021. **Use of Difatsil ["Trasentin"] in Treatment of Obliterative Endarteritis.** (Опыт лечения дифацилом больных облитерирующим эндартеритом в условиях клиники и амбулатории)

A. A. Kozyreva. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 44–48, April, 1955. 17 refs.

Many measures have been suggested to break the pathological link between the central nervous system and the foci of structural change in the peripheral vessels. Some of these have been surgical, others pharmacological, and of the latter, one is "trasentin", known in the U.S.S.R. under the name of "difatsil". In extensive investigations of this compound Anichkov has shown that in addition to its spasmolytic properties it possesses an anaesthetizing and ganglion-blocking effect, and also some indirect ability to stabilize the equilibrium of the stimulating and inhibitory processes of

the cerebral cortex. Further pharmacological properties of this substance as reported by various authors are briefly reviewed. In particular Rodyonov has shown its efficacy in obliterative endarteritis when injected as a 1% solution for blockade of the 2nd and 3rd lumbar sympathetic ganglia for circulatory disturbances of the lower limbs, and of the 2nd and 3rd dorsal ganglia in cases involving the upper extremities.

The present author gave difatsil in doses of 0·1 g. twice daily by mouth (on the fasting stomach) over a period of 3 weeks. She classifies her cases in three stages—ischaemic, dystrophic, and necrotic. In all stages improvement was observed after administration of the drug, as shown by a rise in the temperature of the extremities, improvement in the colour of the skin, and diminution of sweating, and also by capillaroscopic observations. The oscillogram, however, showed little change, except in cases in the first stage. The improvement usually lasted from 6 to 18 months, and no relapses occurred earlier than 6 months after treatment. In all, 105 cases were studied, of which 33 were in the first stage, 59 in the second, and 13 in the third or necrotic stage.

L. Firman-Edwards

1022. **A Combined Treatment of Obliterative Endarteritis.** (Комплексное лечение больных с облитерирующим эндартериитом)
S. S. Remennik. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 38–44, April, 1955. 5 refs.

The author states that the failure of the treatment of obliterative endarteritis in the past has been due to ignoring the vital role played by disturbances of corticovisceral regulation in the production of the disease. In his view treatment must have three main objects: (1) normalization of the higher (cortical) centres; (2) treatment of the most vulnerable peripheral foci; and (3) the breaking of the nervous arcs through which the pathological process is maintained.

The fundamental principle of the author's method is the induction of continuous narcosis for 2 or 3 weeks, during which sleep is maintained for 12 to 15 or even 20 hours a day. This is achieved by administration of 0·8 g. of amylobarbitone and 0·25 g. of phenobarbitone per day for the first week, the dose being halved in the second week; in some cases it was found necessary to give as much as 3 g. of amylobarbitone a day. Sodium bromide is given in the third week. More recently he has used a mixture of 0·1 g. of phenobarbitone and 0·3 g. each of barbitone sodium and amidopyrine. He claims good results from the use of this method alone, but in some cases has supplemented it with the intra-arterial injection of procaine with morphine [dose is not specified] and 100,000 to 200,000 units of penicillin, or alternatively with intravenous injections of 40% glucose and thiamine.

In the last 3 years 45 cases have been treated, 11 by continuous narcosis alone and 34 by the combined treatment, with good results in 28 and satisfactory results in 13; in 4 cases the treatment was ineffective, and 3 patients required amputation of one or more limbs. In the improved cases necrotic foci and ulcers healed, pain diminished or disappeared, and the limbs became warm and of normal colour. The duration of treatment varied with the stage of the disease, in the first stage averaging 28 days, while in the later stages it continued for 61 days. In 20 patients the improvement has lasted over a year —2½ years in some. In 6 cases the condition recurred and in 2 of these, after a second unsuccessful course of treatment, amputation at the thigh was performed.

L. Firman-Edwards

PULMONARY CIRCULATION

1023. **Acute Hemodynamic Effects of Hexamethonium (C6) in Patients with Emphysematous Pulmonary Hypertension**
S. M. Sancetta. *American Heart Journal* [*Amer. Heart J.*] **49**, 501–506, April, 1955. 10 refs.

From Western Reserve University, Cleveland, Ohio, the author describes the haemodynamic effects of the administration of hexamethonium to 8 male patients, aged from 53 to 69 years, with well-established emphysema but without complications. All observations were made with the patient in the horizontal posture, since on a previous occasion the administration of hexamethonium to 3 emphysematous patients in the upright position had led to almost immediate loss of consciousness. By means of cardiac catheterization the right atrial, ventricular, pulmonary arterial, and brachial arterial pressures were recorded on a Brush multichannel oscillograph. Cardiac output was calculated by the direct Fick method, and total pulmonary and estimated total peripheral resistances were calculated from standard formulae. The hexamethonium was given in a dose of 50 mg. through the catheter during a 15-minute period and blood-pressure readings were taken 20 minutes later and compared with those obtained before the administration of the drug. Ten healthy subjects acted as a control group.

The findings, which are tabulated, showed that both in the normal controls and in the emphysematous subjects there was a fall in the brachial and pulmonary arterial pressures and in the estimated total peripheral resistance. The total pulmonary resistance decreased in the normal subjects after the administration of hexamethonium, but not in the emphysematous patients. In the latter there was a significant fall in cardiac output, associated with an absence of the normally observed increase in the heart rate. In the author's view, this lack of cardiac acceleration (which he is unable to explain) is responsible for a decrease in venous return, leading to some decrease in pulmonary arterial pressure. The resulting decrease in pulmonary blood flow did not, however, give rise to increased total pulmonary resistance, as might have been expected. It is suggested that dilatation of pulmonary vasomotor elements may have accounted for this phenomenon.

It is concluded that clinically there is no place for hexamethonium in the treatment of emphysematous subjects, the reduction in pulmonary hypertension being offset by the fall in systemic blood pressure and cardiac outsut.

H. F. Reichenfeld

Haematology

1024. **Assessment of Blood-loss in Civilian Trauma**
R. CLARKE, E. TOPLEY, and C. T. G. FLEAR. *Lancet* [*Lancet*] **1**, 629–638, March 26, 1955. 2 figs., 18 refs.

In cases of accidental injury the assessment of the amount of blood lost, made on a basis of the general clinical state, is far from easy, but accurate assessment may be important, especially if surgical treatment necessitating some further loss will be required. In cases of closed injuries the blood loss may be, and generally is, underestimated. In this paper from the Birmingham Accident Hospital the authors describe attempts made to assess blood loss, mainly by indirect means.

In closed injuries of the limbs such as simple fracture a rough estimate of internal blood loss may be obtained from measurement of the initial swelling, and the general accuracy of such estimates may be checked by determination of the erythrocyte volume, reduction in which requires no transfusion and is not relevant to the production of shock. In more extensive or compound fractures of the tibia and fibula or femur and in severe fractures in the upper limb blood loss is difficult to assess. In such cases the loss may amount to 10 to 30% of the total blood volume, that is, 0·5 to 1·5 litres of blood, while multiple fractures and severe fractures of the pelvis may result in a loss of 40 to 50% of total blood volume, and may moreover be associated with some loss of blood to the exterior. The amount of external bleeding is often impossible to assess, but an effort should be made to gain information of its degree by noting the amount of blood in the clothing or if possible on the road at the scene of the accident. However, the only reasonably accurate estimate is that obtained from determination of blood volume and haemoglobin value. The accompanying case histories, diagrams, and photographs are clear, and useful methods of investigation are described. A number of tables show how the cruder clinical tests compare with more elaborate methods. [Perhaps the most useful point brought out by this study is that blood loss, especially in closed wounds, is nearly always underestimated.] *R. Weeden Butler*

1025. **Antihemophilic Factor (AHF) Levels following Transfusions of Blood, Plasma and Plasma Fractions**
R. S. LANGDELL, R. H. WAGNER, and K. M. BRINKHOUS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **88**, 212–215, Feb., 1955. 2 figs , 8 refs.

The object of the investigations here described from the University of North Carolina, Chapel Hill, North Carolina, was (1) to determine the extent to which injected antihaemophilic factor (A.H.F.) persists in the circulation of normal and of haemophilic subjects, and (2) to study the effect of different plasma levels of A.H.F. on various tests of clotting efficiency, namely, the whole-blood clotting time, prothrombin utilization test, and the partial thromboplastin time test. The first two procedures are well known; the third test, which can be modified to provide an assay of A.H.F. activity, is described in detail by the authors elsewhere (*J. Lab. clin. Med.*, 1953, **41**, 637). It is dependent on the use of a preparation of cephalin as thromboplastin; this, however, is an incomplete thromboplastin, in that it contains only the lipid component. The clotting time of haemophilic plasma determined with the use of cephalin is considerably longer than that of normal plasma, and a dilution curve for the assay of A.H.F. can be prepared by performing the test on a series of different mixtures of normal and haemophilic plasma.

The present study was carried out on 2 human and 11 canine haemophiliacs and 2 normal dogs. All the subjects received transfusions of homologous blood or plasma, and the dogs were also given transfusions of plasma fractions rich in A.H.F. Before transfusion of the dogs a volume of blood approximately equal to that being administered was withdrawn in an attempt to minimize increase in blood volume. The study showed that the rise in plasma A.H.F. level as a result of transfusion was directly proportional to the amount of A.H.F. administered. Over half its activity had disappeared within a few hours, although traces were shown to persist for nearly a week. Thus, to maintain plasma A.H.F. levels at even 5 to 10% of normal would require frequent replacement transfusion. The injection of plasma fractions rich in A.H.F. into non-haemophilic dogs raised the plasma A.H.F. level to above normal for up to 18 hours, but half of this increase disappeared in 2 to 3 hours, indicating that the rapid utilization of A.H.F. in haemophiliacs is not dissimilar from that in normal subjects. The hypothesis that in haemophilia A.H.F. is produced in normal amounts but for some reason forms an inactive complex with an inhibitor is discussed. The partial thromboplastin test was shown to be a more sensitive index of the plasma A.H.F. level than tests of whole-blood clotting time or prothrombin utilization.
A. S. Douglas

1026. **Desacetylmethylcolchicine in Treatment of Myeloid Leukaemia**
B. J. LEONARD and J. F. WILKINSON. *British Medical Journal* [*Brit. med. J.*] **1**, 874–877, April 9, 1955. 2 figs., 7 refs.

Desacetylmethylcolchicine (" colcemid "), which is isolated from an extract of the mixed alkaloids of *Colchicum autumnale*, was given by mouth to 8 patients with chronic myeloid leukaemia, 6 with acute myeloid leukaemia, one with chronic lymphatic leukaemia, and 2 with myelofibrosis at the Manchester Royal Infirmary. The dosage was 3 mg. daily, increasing to 10 mg. daily, for 3 to 4 weeks. Rapid reduction of splenomegaly, reduction in total leucocyte count to

within normal limits, increase in haemoglobin level, and marked clinical improvement were observed in 6 of the cases of chronic myeloid leukaemia. In the case of chronic lymphatic leukaemia the drug aggravated the condition to the verge of acute relapse. In the cases of myelofibrosis an early fall in leucocyte count and moderate clinical improvement were observed. Residual primitive cells persisted in the blood and marrow even in cases showing the best response to treatment. Any subsequent delay in initiating maintenance treatment tended to result in relative refractoriness. Side-effects were minimal, and thrombocytopenia and aplastic anaemia were not encountered. *Mary D. Smith*

1027. **Histiocytic and Monocytic Leukemia. A Clinical, Hematological, and Pathological Differentiation**
H. W. BELDING, G. A. DALAND, and F. PARKER. *Cancer* [*Cancer* (*N.Y.*)] **8**, 237–252, March–April, 1955. 10 figs., 24 refs.

A detailed description is given of the differences between the two types of so-called monocytic leukaemia, it being held that the Schilling type is really histiocytic leukaemia. Among a series of 21 cases, mainly from the Boston City Hospital, most of the 13 cases of true monocytic leukaemia had a much higher total leucocyte count than those of the histiocytic type, in which leucopenia was common. Extramedullary infiltration seemed to be more extensive in histiocytic leukaemia and the splenomegaly usually greater. Clinically, intercurrent infection and haemorrhage were commoner in monocytic leukaemia.

The authors give a good description of the morphological differences that distinguish monocytes from histiocytes [but the photomicrographs give no useful information]. *A. Piney*

1028. **Respiratory Obstruction in Acute Leukaemia**
V. B. LEVISON. *Lancet* [*Lancet*] **1**, 1151–1152, June 4, 1955. 3 figs., 10 refs.

ANAEMIA

1029. **Elliptocytosis with Hemolytic Anemia: the Effects of Splenectomy**
E. L. LIPTON. *Pediatrics* [*Pediatrics*] **15**, 67–83, Jan., 1955. 7 figs., 46 refs.

In this paper are described the results of a clinical and laboratory investigation of an infant believed to be suffering from congenital elliptocytosis in the homozygous state. Both parents, who were first cousins, also exhibited the elliptocytic trait. The patient had a severe haemolytic anaemia and needed repeated blood transfusions; erythrocytes survived normally after transfusion, but the survival of the patient's cells in a normal recipient was diminished.

In films made from the patient's blood the erythrocytes showed marked variation in size and shape, with many spherocytes and microelliptocytes, and there was evidence of budding and fission. Osmotic fragility was markedly increased. Detailed measurements of the patient's erythrocytes and those of 8 relatives are presented. Splenectomy was performed and led to marked clinical improvement, but it is thought that minimal (compensated) haemolysis persisted.

The author reviews from the haematological, genetic, and therapeutic aspects the scanty reports in the literature on severe haemolytic anaemia in elliptocytosis. He concludes that a homozygous state is not always found, and that incomplete penetrance or a combination with other abnormal genes may explain the haemolysis in heterozygous cases. He suggests that splenectomy should be carried out on all patients with elliptocytosis and overt haemolytic anaemia. *J. V. Dacie*

1030. **Sickle-cell Trait in South Turkey**
M. AKSOY. *Lancet* [*Lancet*] **1**, 589–590, March 19, 1955. 26 refs.

At the State Hospital at Mersin in southern Turkey sickle-cell anaemia was diagnosed in 15 individuals, all of whom belonged to a community which had been established centuries ago by immigrants from Syria and Egypt. Of 376 members of this community whose blood was investigated, 50 were found to be carriers of the sickling gene. Of 200 native Turks serving as a control group, none showed the abnormality. *H. Lehmann*

1031. **Surface Scintillation Measurements in Humans of the Uptake of Parenterally Administered Radioactive Vitamin B_{12}**
G. B. J. GLASS, L. J. BOYD, and G. A. GELLIN. *Blood* [*Blood*] **10**, 95–114, Feb., 1955. 7 figs., 25 refs.

The authors describe observations carried out at the Flower and Fifth Avenue Hospitals (New York Medical College), New York, on the distribution of vitamin B_{12} (cyanocobalamin) in man by making scintillation counts of radioactivity over skin projections of various organs after the parenteral injection of radioactive vitamin B_{12}. They point out that complicating factors such as the presence of secondary and back-scattered radiation and the absorption of radiation in the tissues make the quantitative interpretation of results almost impossible, but suggest that the evaluation of patterns of distribution is possible and useful.

In 2 control subjects over 96% of the dose of radioactive vitamin B_{12} was lost from the site of intramuscular injection within 4 hours, during which time peak values were reached over the spleen, kidney, and iliac crest. Peak values in the liver were reached only after 5 to 6 days, and the decline was slow and small, persisting at about 86% of the peak value 2 to 3 months after injection. This prolonged storage in the liver perhaps explains the long time needed for the depletion of hepatic stores of the vitamin—for instance, after total gastrectomy—and the long remissions observed in cases of untreated pernicious anaemia. The pattern of uptake of the vitamin in a patient with total gastrectomy was grossly similar to that observed in normal controls. In a patient with pernicious anaemia in partial remission the uptake in the kidney and spleen was rather higher than in the controls and that in the liver approximately the same, but the values observed over the iliac crest showed a significantly

faster decline. Observations on a larger number of patients are required before these variations between different disease patterns can be accepted as significant.

Janet Vaughan

1032. **An Apparently Homogeneous Substance with Intrinsic-factor Activity Associated with Cell Particles from Human Stomach**

J. R. P. O'Brien, W. H. Taylor, A. L. Turnbull, and L. J. Witts. *Lancet* [*Lancet*] **1**, 847–848, April 23, 1955. 5 refs.

In this preliminary communication from the Radcliffe Infirmary, Oxford, the authors describe the isolation from human gastric mucous membrane of a substance showing activity similar to that of Castle's intrinsic factor. Stomachs removed at operation for duodenal ulcer were placed immediately in a vessel surrounded by a mixture of ice, salt, and water. The mucous membrane was then stripped, washed with isotonic saline at 0° to 5° C., cut into pieces 0·5 sq. cm. in area, and extracted with 2% (w/v) saline solution in a macerator at less than 12° C. for 5 minutes. After centrifugation at 2,000 r.p.m. for 20 minutes, the pale red supernatant was frozen and stored for up to 2 months until sufficient material had been accumulated.

Pooled material was subjected to 38,000 *g* in an ultracentrifuge for 10 minutes. The precipitate, consisting of microsomes, mitochondria, and damaged cells, was resuspended in ice-cold distilled water, stirred intermittently for 10 minutes, and again centrifuged for 20 minutes at 2,000 r.p.m. The now colourless supernatants from this and two further extractions were mixed and dialysed at 0° to 5° C. against water distilled in glass until free from chloride ions, the resultant flocculent precipitate being removed by centrifugation and discarded. After concentration of the supernatant to one-fifth of its volume against 20% dextran in water (the consequent flocculent precipitate again being discarded), the pale yellow powder obtained after freeze-drying was found to be electrophoretically and ultracentrifugally homogeneous.

Its power to act as intrinsic factor was evidenced by the ability of 10 mg. to promote the absorption of 32% of an orally administered dose of 0·5 μg. of vitamin B_{12}, labelled with radioactive cobalt, in patients with pernicious anaemia. It was, however, much less active and of higher molecular weight (40,000) than intrinsic factor isolated from gastric juice, of which, it is thought, it may be a precursor.

M. Sandler

1033. **The Response of Megaloblastic Anaemia of Pregnancy to Vitamin B_{12}**

H. C. Moore, E. W. Lillie, and P. B. B. Gatenby. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] 106–116, March, 1955. 29 refs.

The authors, from the Rotunda Hospital, Dublin, report the results of treatment of 17 cases of megaloblastic anaemia of pregnancy with vitamin B_{12} (cyanocobalamin) given intramuscularly in a dose varying from 20 to 1,000 μg. daily. for variable periods ranging from 5 to 24 days. In 4 cases treatment was started in the antenatal period and in 12 cases between 4 and 28 days after delivery. Iron was given by mouth to 6 of the patients during the period of vitamin-B_{12} therapy.

In 13 of the 17 cases a reticulocyte response and haematological improvement were noted, the reticulocyte peak varying from 5 to 21% and occurring between 4 and 27 days after the beginning of treatment. No relationship was found between the dosage and the height of the peak. In 4 of the 13 cases a second reticulocyte rise did not occur after administration of folic acid. The 4 cases in which there was failure to obtain a reticulocyte response after a total dose of 680 to 5,000 μg. of vitamin B_{12} had been given responded to treatment with 20 mg. of folic acid daily.

Of the 6 cases in which fat balance studies were carried out, none showed defective absorption.

D. G. Adamson

1034. **The Auto-immune Hemolytic Anemia of Malignant Lymphocytic Disease**

M. C. Rosenthal, A. V. Pisciotta, Z. D. Komninos, H. Goldenberg, and W. Dameshek. *Blood* [*Blood*] **10**, 197–227, March, 1955. 4 figs., bibliography.

In this comprehensive paper from the New England Center Hospitals and Tufts College Medical School, Boston, are reviewed the clinical, haematological, and serological findings in 24 cases of auto-immune haemolytic anaemia associated with malignant lymphatic disease, in the form of lymphosarcoma in 4 cases and of chronic lymphatic leukaemia in the remainder. In about half the cases the development of haemolytic anaemia led to the lymphatic disease being discovered; in the others lymphatic leukaemia was well established before signs of haemolysis were detected, and in some of these *x*-ray therapy appeared to have precipitated the haemolysis. The laboratory findings were identical with those found in " idiopathic " auto-immune haemolytic disease, except for the presence of signs of lymphocyte proliferation; in particular, the direct Coombs test was positive in all of 20 patients tested, and abnormal haem-agglutinins were demonstrated in the serum of 11 out of 19 patients investigated. The authors also noted the occurrence in other patients of " occult " haemolysis, which was not apparently due to auto-immunization and was detected only by the finding of a shortened erythrocyte survival time and an increased faecal output of urobilinogen.

The pathogenesis is discussed, in particular the possibility that the lymphocyte may act as an antigen in these cases. In regard to treatment the authors suggest that the haemolytic element should be treated independently of the lymphocytic proliferation. The use of ACTH and Compound E or F is recommended, with blood transfusion and splenectomy as ancillary aids when hormone therapy is unsuccessful. In 2 patients out of 10 who underwent splenectomy the operation was successful, one patient having complete remission for over 4 years, while in 2 others the rate of haemolysis was considerably diminished.

J. V. Dacie

See also Tropical Medicine, Abstracts 972–3.

Respiratory System

1035. **An Analytical Review of Spontaneous Haemopneumothorax**
R. J. CALVERT and E. SMITH. *Thorax* [*Thorax*] **10**, 64–72, March, 1955. 7 figs., bibliography.

The authors describe 3 cases of spontaneous haemopneumothorax treated at Whipps Cross Hospital, London, during the last 2 years and review the aetiology, pathology, and treatment of this condition. Two of the cases occurred in healthy young adult males, and the third in a woman of 40 years who, apart from rheumatic fever in childhood and a tuberculous ganglion of the wrist, had had no previous illnesses of note. Both men were treated by pleural tapping and recovered; follow-up chest radiographs showed mid-zonal cystic disease in one, the other being normal. The female patient was shocked on admission and died despite massive blood transfusion. At necropsy a stretched and torn apical pleural adhesion, which was regarded as tuberculous, was found.

Caution in the use of intrapleural instillation of streptokinase and streptodornase is enjoined by the authors because of the pyrexial episodes engendered. They regard massive haemorrhage as a surgical rather than a medical emergency, and advise early thoracotomy, with ligation or electrocoagulation of any bleeding points found, as the treatment of choice. They consider that the guide to intervention should be the pulse rate rather than the blood pressure. *I. M. Librach*

1036. **Mediastinal Emphysema and its Occurrence in Artificial Pneumoperitoneum**
C. S. BREATHNACH. *Thorax* [*Thorax*] **10**, 79–84, March, 1955. 2 figs., 46 refs.

From the Rialto Chest Hospital, Dublin, the author describes the occurrence of subcutaneous and mediastinal emphysema as a complication of artificial pneumoperitoneum in 3 young patients (2 men and one woman) suffering from pulmonary tuberculosis. The phenomenon occurred in 2 cases as a result of sudden straining, retching, and coughing after the pneumoperitoneum had been established for some time. In the third case, that of a man of 22, it appeared spontaneously 3 hours after a normal induction with 600 ml. of air, a pressure of 8 mm. H_2O being present after the procedure was completed; it recurred one month later. In all cases the emphysema subsided spontaneously, but refills were discontinued. The author concludes that a rise in intraperitoneal pressure as a result of the strain of coughing or retching causes an escape of peritoneal air through the para-oesophageal orifice in the diaphragm into the mediastinum, whence it finds its way into the neck via the cervico-mediastinal perivisceral fascial spaces. The condition is described as "malignant" if the air is enclosed within the inner fascial spaces and its escape into the soft tissues of the neck prevented, or if excess air enters the mediastinum, as from a fistulous communication with a hollow intrathoracic viscus, mediastinal compression often causing a fatal outcome in such cases if the tension is not relieved by incision of the perivisceral fascia above the thyroid isthmus. In the benign type the air infiltrates outside the boundaries of the perivisceral fascia and is able to diffuse much more widely. A combination of both types may also occur.
I. M. Librach

1037. **Endobronchial Placer Mining for Neoplastic Cells**
J. B. GREGG, B. M. MERKEL, and K. R. CROSS. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **61**, 267–276, March, 1955. 6 figs., bibliography.

In "placer-mining" for gold a powerful stream of water is used to drive gold particles into a container for collection. The authors use a similar method to increase the cellular content of specimens obtained from the bronchial mucosa for cytological examination. The most likely area is first determined radiologically. After bronchoscopic examination and removal of a fragment of the mucosa with forceps if possible, the abraded area is irrigated and the fluid removed by suction. If a piece cannot be removed with forceps, the mucosa in the suspected area is abraded with the tip of the suction tube. The washings are centrifuged, and the deposit fixed and sections made in the usual way. Mucus from a suspected bronchiole is removed and treated in the same way. The only complication noted among 190 cases was pneumothorax, which appeared 24 hours after the examination in one case and subsided on conservative treatment. Subsequent bronchoscopy of 22 patients showed no evidence of residual injury.
F. W. Watkyn-Thomas

1038. **Is Survey Cancer of the Lung Curable?**
K. R. BOUCOT and M. J. SOKOLOFF. *Diseases of the Chest* [*Dis. Chest*] **27**, 369–388, April, 1955. 7 figs., 14 refs.

A significant number of cancers of the lung are being detected by mass surveys, and the authors, considering that "the fate of primary bronchogenic carcinoma cases detected at these units may help illuminate the role of surveys in finding curable lung cancer", studied 100 consecutive cases recognized radiologically in two Philadelphia survey units from January, 1947, to May, 1953. Exploration was carried out in 52 instances, but resection was possible in only 30. Immediate operative mortality was 17%. Detailed survival studies of the 57 cases surveyed up to August, 1950, suggest a graver prognosis for patients under 55, those whose radiograph obviously indicated neoplasm or tuberculosis, those with respiratory symptoms severe enough to have caused them to seek advice, those with bronchoscopic abnormality of any type, those with undifferentiated carcinoma, and those with concomitant active tuberculosis. Of the 100 cases, 10 had concomitant active pulmonary tuberculosis; none of these patients survived. The authors

stress the danger of failing to bear in mind the increasing association of these two diseases in older men. Even when the diagnosis of active tuberculosis is proved by the repeated finding of tubercle bacilli in the sputum they consider that exploration should be carried out in all men over 45 with radiological evidence of tumour.

Of the 57 patients surveyed up to 1950, with a minimum follow-up period of 3 years, only 5 (9%) had undergone resection and were alive 3 years after radiological abnormality was first found. Four of these 5 patients, who were aged between 58 and 65, had squamous carcinoma and one an adenocarcinoma; 4 had no symptom troublesome enough to cause them to seek advice, and not one had been admitted to hospital within 3 months after the first finding of abnormality. Paradoxically, the fate of patients admitted within 3 months of their first abnormal radiograph was worse than that of those whose admission was delayed more than 3 months. This was probably due to the fact that cases admitted as emergencies were usually advanced beyond saving and that the prognosis is better in those with radiologically inconspicuous lesions. Five-year survival rates are not yet available for a significant number of cases, but there is little reason to expect that such rates in survey-detected cases will be better than the 9% in resected cases.

The following suggestions are made for increasing the usefulness of surveys: (1) When persistent or unusual respiratory symptoms are present, men over 45 should be referred for diagnostic study rather than for survey radiography. (2) Men over 45 with no respiratory symptoms should report for radiological examination every 6 months. (3) Survey radiographs should be more carefully read, as unimpressive lesions may be as significant as dramatic ones, especially if due to tuberculosis or cancer. (4) When any abnormality is found in the chest radiograph of a man over 45 cancer should immediately be suspected and the patient admitted to hospital. At present admission is generally limited to those with positive evidence of neoplasm. (5) The possibility that cancer of the lung may accompany pulmonary tuberculosis should always be remembered.

The authors, in concluding that in cancer of the lung survival is apparently limited to cases with a slow-growing tumour, suggest that " there is a fertile field for investigation of factors related to rate of tumor growth ".

D. P. McDonald

1039. **Generalized Hypertrophic Osteoarthropathy in Association with Bronchial Carcinoma. A Review, Based on 24 Cases**

T. SEMPLE and R. A. MCCLUSKIE. *British Medical Journal* [*Brit. med. J.*] **1**, 754–759, March 26, 1955. 3 figs., 41 refs.

The clinical significance of joint symptoms associated with signs of hypertrophic pulmonary osteoarthropathy in the diagnosis of bronchial carcinoma is discussed, with reference to 24 cases seen over a period of 7 years in the West of Scotland. The authors noted that joint symptoms were sometimes present as long as 16 months before the diagnosis was established, the pain and deformity often being crippling. In many of the cases symptoms were dramatically relieved by removal of the tumour and bony changes often regressed. After discussing possible causative factors of the syndrome, including endocrine disturbances, hormonal secretion by the tumour, and an autonomic pulmonary–systemic vascular reflex, the authors conclude that carcinoma of the bronchus, often of a peripheral and therefore " silent " type, is the commonest cause of hypertrophic osteoarthropathy.

J. Robertson Sinton

1040. **The Effect of Breathing 100 per cent Oxygen in Pulmonary Emphysema: Correlation of Clinical Improvement with Changes in Pulmonary Ventilation**

H. A. BICKERMAN and A. L. BARACH. *Journal of Chronic Diseases* [*J. chron. Dis.*] **1**, 111–120, Feb., 1955. 14 refs.

This report from the Goldwater Memorial Hospital (Columbia University), New York, elaborates the earlier work of Barach (*Ann. intern. Med.*, 1938, **12**, 454), who showed that a fall in minute pulmonary ventilation occurred immediately in emphysematous subjects on breathing pure oxygen. In the present study resting ventilation was measured, with the subject seated, by means of a Benedict–Roth spirometer, and straight-line tracings were obtained by continuously replacing the oxygen consumed from a reservoir spirometer. The 121 patients tested, who suffered from emphysema but were free from cardiac failure, were grouped clinically according to the severity of their symptoms into four grades of increasing severity.

The proportional decrease in pulmonary ventilation in the four groups on changing from air to oxygen was as follows: Grade I, 8%; Grade II, 18%; Grade III, 21%; and Grade IV, 23%. In 4 cases in which blood gas analysis was performed there was a correlated rise in arterial oxygen saturation. In asthmatic patients the ventilation fell by 2·6% and in normal subjects it rose by 1·4%, but these figures are not statistically significant. Pulmonary ventilation was then determined while the subjects were breathing air in the head-down position at an angle of 15 degrees. The mean reduction in three different groups was as follows: patients with emphysema, 17·5%; with asthma, 7·5%; and normal subjects, 3·4%. The fall in emphysematous subjects was of the same order as that which they showed on breathing oxygen, and is ascribed to increased aeration of the lower lobes. Determination of the ventilatory equivalent (expressed in ml. of oxygen consumed per litre of ventilation per sq. metre of body surface area) showed that this value rose 17% in emphysematous subjects when oxygen was substituted for air and when air was breathed in the head-down position, but no consistent pattern of change was noted in normal and asthmatic subjects under similar conditions.

Finally, 33 patients with severe emphysema (Grades III and IV) were given 2 to 6 months' training in diaphragmatic breathing, combined with treatment by inhalation of vasoconstrictor aerosols and ingestion of spasmolytics. Before training the mean fall in ventilation on changing from air to oxygen inhalation was 22%; after training it was only 8%, and there was in addition a corresponding improvement in exercise tolerance.

Bernard J. Freedman

Otorhinolaryngology

1041. **Intra-arterial Administration of Penicillin in Treatment of Acute Mastoiditis**
S. NAKAMURA and K. NAGANUMA. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **61**, 61–66, Jan., 1955. 7 figs., 2 refs.

The treatment of acute mastoiditis by the injection of penicillin into the common carotid artery is described in this paper from Nihon University College of Medicine, Tokyo. The common carotid artery on the affected side is exposed and penicillin injected in doses of 600 units per kg. body weight at intervals of 3 to 6 hours to a total of 180,000 to 400,000 units. Observations on rabbits and human subjects showed that the concentration of penicillin in the aural discharge was much greater after intracarotid than after intramuscular injection, and it is claimed that the need for mastoidectomy is markedly reduced by this method of treatment. Of 24 patients treated by the authors, all but 3 were cured without operation, most of them having completely recovered within 3 weeks.

[The authors do not state why they regard multiple injections into the carotid artery as preferable to an ordinary mastoidectomy, nor do they mention the possible effect of such injections on the artery.]

F. W. Watkyn-Thomas

1042. **Fenestration—Past, Present and Future**
G. E. SHAMBAUGH. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol.* (*St Louis*)] **64**, 149–160, March, 1955. 8 figs., 22 refs.

After a brief historical survey, with particular reference to the early work of Sourdille, Mosher, and Lempert on the treatment of otosclerosis, the author states his belief that the future of the fenestration operation should include methods of overcoming postoperative serous labyrinthitis, of restoring the small conductive loss which seems to be inevitable even in cases in which the operation has been a success, and of gaining information about the improvement in hearing many years after the performance of fenestration.

The most serious cause of failure at present is postoperative serous labyrinthitis, the cause of which is still unknown. Juers in 1948 obtained a slight increase in hearing in the fenestrated ear by blocking the tympanic membrane, and some similar method of altering the balance between the fenestra and the round window may improve the result from fenestration still further. In one series of 390 cases the author, with Adin (*Arch. Otolaryng.* (*Chicago*), 1951, **53**, 243), was able to report that the hearing improvement in 273 (70%) was maintained 5 to 10 years after operation. There is some suggestion that the cochlear nerve degenerates less quickly after a successful fenestration, but this is still to be confirmed. As an alternative to fenestration it is suggested that new developments in the operation of mobilization of the stapes hold some promise, but its success is still to be proved. The author recalls that as long ago as 1893 Jack remarked that "mobilization of the stapes gives results for a few weeks and then the adhesions reform and the trouble returns".

William McKenzie

1043. **Labyrinthine Surgery in the Treatment of Ménière's Disease**
J. R. LINDSAY and K. H. SIEDENTOP. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol.* (*St Louis*)] **64**, 69–78, March, 1955. 18 refs.

At the otolaryngological clinics of the University of Chicago during the period 1940–54 less than 10% of patients suffering from Ménière's disease were referred for operation. The results of surgical treatment as reported by many other workers are briefly reviewed and some experimental work on monkeys is described. The authors state that the various surgical methods of destruction of the labyrinth have not proved satisfactory, and recently they have devised a more radical method in which the ampullary ends of the horizontal and superior vertical canals are removed and the vestibule destroyed through the opening made into the bony labyrinth. Operation by this method in 4 cases followed up for 6 months to 2 years has given "uniformly good" results; hearing has been totally destroyed, but attacks of vertigo have been abolished and tinnitus relieved in all 4 cases.

William McKenzie

1044. **The Efficacy of Nasopharyngeal Irradiation for the Prevention of Deafness in Children.** [In English]
J. E. BORDLEY and W. G. HARDY. *Acta oto-laryngologica* [*Acta oto-laryng.* (*Stockh.*)] Suppl. 120, 1–49, 1955. 6 figs., 8 refs.

1045. **Bilateral Abductor Paralysis of the Larynx. Results of Treatment by Modified King Operation**
L. H. CLERF. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol.* (*St Louis*)] **64**, 38–46, March, 1955. 2 refs.

The fundamental principle of the operation described by King (*J. Amer. med. Ass.*, 1939, **112**, 814) is mobilization and lateral fixation of an arytenoid. The present author has employed this operation, with slight modification, in the treatment of 103 patients with bilateral abductor paralysis of the larynx following thyroidectomy and 9 others in which it was due to other causes. The postoperative complications and end-results are here discussed.

In the majority of cases the arytenoid was fixed to the wing of the thyroid cartilage. In only 11 cases was it impossible to remove the tracheotomy cannula after operation, and in 4 of them this involved performance of King's operation on the opposite side. In cases in which the paralysis had not occurred as a complication of thyroidectomy a good result from the operation was less certain.

William McKenzie

Urogenital System

1046. **Mechanism of Cardiac Changes Observed in Uremia**

M. M. GERTLER, J. KREAM, and J. HYLIN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **88**, 439–440, March, 1955. 1 fig., 16 refs.

At the Columbia–Presbyterian Medical Center, New York, the cardiac changes due to uraemia were studied in 8 dogs made uraemic by ligation of the ureters. They were then killed, the heart removed and freed of blood and epicardial fat, and portions of ventricular muscle were homogenized and assayed for cholinesterase activity by Ammon's method. Ventricular muscle from 6 normal control animals was similarly assayed.

It was shown that the cholinesterase activity of ventricular muscle from the uraemic dogs was consistently and significantly lower than that in the controls. It is suggested that this depressed cholinesterase activity could account for some of the electrocardiographic abnormalities, such as various degrees of heart block, seen in patients with uraemia. *K. G. Lowe*

1047. **Post-traumatic Renal Insufficiency in Military Casualties. I. Clinical Characteristics. II. Management, Use of an Artificial Kidney, Prognosis**

P. E. TESCHAN, R. S. POST, L. H. SMITH, R. S. ABERNATHY, J. H. DAVIS, D. M. GRAY, J. M. HOWARD, K. E. JOHNSON, E. KLOPP, R. L. MUNDY, M. P. O'MEARA, and B. F. RUSH. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 172–186 and 187–198, Feb., 1955. 6 figs., bibliography.

Writing from the U.S. Army Medical Service Graduate School, Washington, D.C., the authors discuss the incidence, aetiology, and treatment of post-traumatic renal insufficiency, with special reference to 51 patients with oliguria (urine volume less than 500 ml. per day) but without hypotension or dehydration, who were admitted during 1952 to a special "renal insufficiency center" established behind the Korean battle-front; the average time of admission after wounding was 3·2 days. The incidence of oliguria among surviving casualties at the forward hospitals was about 0·5%. The development of oliguria in these patients could not be related to delay in evacuation from the front line to forward hospitals (average time 4·6 hours), but possible important factors were the duration of hypotension, inadequate blood replacement, and severity of the wounds sustained.

Nearly all these patients showed a steeper rise in the plasma potassium level than is usual in oliguric patients seen in civilian practice. They also showed clinical signs of uraemia unduly early, wasted rapidly, and developed oedema owing to the large amounts of water released from catabolized tissues. Impaired wound healing, a tendency to bleeding, and increasing anaemia were common clinical features. Hypertension was noted in 36 (85%) of 42 cases. The patients were kept in approximate fluid balance so adjusted as to produce a steady decrease in body weight. At least 100 g. of glucose was given daily, latterly as a 50% solution into a major vein. An average of about 5 litres of blood was required to combat anaemia during the oliguric period. Dialysis with a Brigham–Kolff artificial kidney was carried out 72 times on 31 patients, usually on account of hyperkalaemia or severe clinical signs and symptoms of uraemia. Because of the rapid rise in the plasma potassium level in these patients dialysis was instituted when this level rose to between 6·5 and 7·5 mEq. per litre. Occasionally dialysis was carried out in mild cases of uraemia as a prelude to major surgery. The complications of dialysis were fever, rigors, and fluctuations in blood pressure, but only 2 patients had severe episodes of bleeding requiring cessation of dialysis. Of the 31 patients treated by dialysis, 21 died, while of the other 20 patients, 6 died. The over-all mortality was therefore 27 out of 51 (53%). Nearly all the deaths could be related to some complication of the injury, such as infection or secondary haemorrhage. *K. G. Lowe*

1048. **Clinical Management of the Anuric Patient**

H. C. OARD and G. I. WALKER. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 199–206, Feb., 1955. 4 figs., 5 refs.

The authors suggest that in the management of anuric or oliguric patients too much fluid is usually given. They then describe the course of acute renal insufficiency in 4 patients, in 2 cases due to carbon tetrachloride poisoning, in one to transfusion of mismatched blood, and in one to post-partum haemorrhage. Treatment during the oliguric period, which ranged from 9 to 16 days, consisted almost solely in the oral administration of about 500 ml. of 20% lactose solution daily. Any variation in this volume of fluid intake was determined by the patient's feeling of thirst or the appearance of physical signs suggesting over- or under-hydration. No attempt was made to correct plasma electrolyte levels and no elaborate laboratory investigations were deemed necessary. All 4 patients, whose detailed case histories are given, made a good clinical recovery.

K. G. Lowe

1049. **Malarial Therapy in the Nephrotic Syndrome**

A. G. SHAPER. *British Medical Journal* [*Brit. med. J.*] **1**, 1132–1135, May 7, 1955. 7 refs.

At Sefton General Hospital, Liverpool, 7 cases of the nephrotic syndrome were treated by the induction of malaria by exposure to infected mosquitoes, the patient being allowed to have as many rigors as he could tolerate. One patient showed a dramatic response and remained well 18 months later, 2 others improved in respect of the oedema though the progress of the disease was not halted, and the remainder did not improve.

J. McMichael

Endocrinology

THYROID GLAND

1050. **The Effect of *levo*-Thyroxine, *dextro*-Thyroxine and *levo*-Tri-iodo-thyronine on the Electrocardiogram in Myxedema: Preliminary Report**

P. STARR and R. LIEBHOLD-SCHUECK. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 595–606, March, 1955. 6 figs., 7 refs.

It is pointed out that thyroid hormone has a threefold action on the heart in myxoedema: (1) pharmacodynamic, by potentiating the action of adrenaline and noradrenaline; (2) indirect, by increasing the metabolic demands of the body; and (3) direct, by having an effect on the histological changes in the heart muscle. At the Los Angeles County Hospital the effects on the heart of the two optical isomers of thyroxine and of *laevo*triiodothyronine have been compared in cases of myxoedema, sodium *laevo*thyroxine pentahydrate being given in a daily dosage of 0·05 to 0·2 mg., sodium *dextro*thyroxine pentahydrate in a daily dosage of 0·3 to 1·0 mg., and *laevo*triiodothyronine in a daily dosage of 0·0088 to 0·035 mg. Six illustrative cases are described. Before and after administration of the drugs serial electrocardiograms (ECG) were taken and the serum protein-bound iodine level and the basal metabolic rate (B.M.R.) were estimated. It was found that the ECG frequently began to change towards the normal before there was any alteration in the serum protein-bound iodine level or the B.M.R., and the authors therefore propose that changes in the ECG should be used as a guide to dosage of thyroxine in myxoedema rather than the serum protein-bound iodine level or the B.M.R. There was a definite response of the ECG to *dextro*thyroxine but this was less than that observed with an equivalent dosage of *laevo*thyroxine. As was expected, triiodothyronine appeared to have a more marked effect on the ECG than *laevo*thyroxine. It is suggested that a further study of the pharmacodynamic action of thyroxine on the heart is warranted.

G. S. Crockett

1051. **Lack of Effect of Fluorine Ingestion on Uptake of Iodine^{131} by the Thyroid Gland**

J. E. LEVI and H. E. SILBERSTEIN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **45**, 348–351, March, 1955. 10 refs.

The effect of fluoridization of public water supplies on iodine uptake by the thyroid gland was investigated at the Sinai Hospital, Baltimore, there being some evidence which suggests that fluorine can compete with iodine and thus affect the metabolism of the thyroid gland. However, using the uptake of radioactive iodine (^{131}I) as a test of thyroid function, no change could be demonstrated in 17 healthy subjects when 4 mg. of fluoride ion was given daily as sodium fluorosilicate for 10 weeks. It does not seem likely, therefore, that the presence of fluoride in the drinking water in a concentration of 1 p.p.m. will upset thyroid metabolism.

M. C. G. Israëls

1052. **The Use of the Urinary Pigment : Creatinine Ratio as a Measure of Basal Metabolic Rate and Thyroid Activity**

F. B. MORELAND and A. E. GURGIOLO. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **45**, 352–356, March, 1955. 6 refs.

The amount of pigment excreted in the urine has been shown to be proportional to the basal metabolic rate (B.M.R.). Since in the presence of thyroid dysfunction the urinary excretion of pigment and of creatinine vary in opposite directions, the ratio between the two varies more widely than either value alone; its determination has therefore been used as a means of estimating the B.M.R. In the present paper the authors give the details of this method and compare the results obtained by it with those obtained by the standard method in relation to the clinical status and the uptake of radioactive iodine by the thyroid gland in a number of patients with hyperthyroidism or hypothyroidism and in euthyroid subjects.

They conclude that the method described is not as reliable as the measurement of oxygen consumption, but might be of value when, for one reason or another, the oxygen consumption cannot be determined accurately.

M. C. G. Israëls

1053. **Glycine and Synthesis of *para*-Aminohippuric Acid in " Free Anxiety " and Hyperthyroidism**

M. J. MUSSER, W. P. DEISS, and T. H. LORENZ. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **45**, 357–362, March, 1955. 3 figs., 7 refs.

It has been shown that in patients with hyperthyroidism the excretion of hippuric acid following the administration of sodium benzoate is abnormally low, whereas in certain chronic anxiety states, the symptoms of which resemble those of hyperthyroidism, it is abnormally high. The former abnormality has been attributed to liver damage, but since the synthesis of hippuric acid is dependent not only on the conjugating function of the liver, but also on the availability of glycine, the abnormalities observed in both conditions might equally well be due to changes in glycine metabolism. The mechanism of synthesis of *p*-aminohippuric acid (PAH) is similar to that of hippuric acid and is influenced in the same way by glycine. The effect of increasing the availability of glycine on PAH synthesis in these two disorders and in normal subjects was therefore studied at the University of Wisconsin Hospitals, Madison. In 23 subjects with chronic " free anxiety " the rise in serum PAH content, measured colorimetrically, after the administration of 6 g. of sodium *p*-aminobenzoate was

151% of the mean rise found in normal subjects, compared with 71% in 22 patients with hyperthyroidism. When glycine was given in addition the mean rise in serum PAH level in normal subjects was 162% of the previous rise, while in the hyperthyroid subjects the rise increased from 71% to 158% and in the patients with "free anxiety" from 151% to 194% of the original mean rise in normal subjects.

The authors suggest that the reduced level of PAH synthesis and the relatively large increase on giving glycine in hyperthyroid subjects indicate a diminution in the availability of glycine, whereas the high rate of synthesis of PAH and relatively small effect of additional glycine in cases of "free anxiety" reflect increased availability of glycine in such cases. *M. C. G. Israëls*

1054. **The Basal Metabolic Rate during Sleep**
R. FRASER and B. E. C. NORDIN. *Lancet* [*Lancet*] 1, 532–533, March 12, 1955. 3 figs., 3 refs.

Although estimation of the basal metabolic rate (B.M.R.) is one of the simplest ways of measuring the activity of the thyroid gland, it is often difficult to achieve the basal state and obtain reliable and accurate readings. Following the work of Bartels and of Rapport, the present authors have studied the B.M.R. during barbiturate sleep in 126 patients at Hammersmith Hospital, London, hoping to eliminate by this means the sources of error in the standard method. Intravenous pentobarbitone sodium was used to induce sleep in 73 patients, tracings being first obtained without sedation on two successive days, after which the drug was injected in a dose sufficient to put the patient to sleep without reaching the level of surgical anaesthesia and another tracing was taken. The same routine was followed with another 53 patients except that instead of pentobarbitone, amylobarbitone sodium was given by mouth at the rate of 3 gr. (200 mg.) every hour until the patient could no longer be roused. The patients given pentobarbitone were divided on the basis of clinical findings, response to treatment, and the results of radioactive-iodine tests, into six categories—definite and possible myxoedema, euthyroid, definite and possible hyperthyroidism, and "nervous". Those given amylobarbitone, being less numerous, were divided only into hypothyroid, euthyroid, and hyperthyroid groups. Each result was expressed as a percentage of the appropriate standard mean value as determined and reported by Robertson and Reid (*Lancet*, 1952, **1**, 940).

In general, the tracings made during sleep were straighter and smoother than when the patient was awake. With pentobarbitone the rates for euthyroid subjects fell within the normal range (85 to 115%) and were clustered more closely around the mean than the lowest values obtained in the waking state. Similarly the B.M.R. during sleep did not differ greatly from the waking value in any of the other groups except the "nervous", in all of whom the B.M.R., previously high, fell during sleep within the normal range. Similar results were obtained with amylobarbitone.

The authors conclude that estimation of the B.M.R. during sleep eliminates the effect of nervousness, which is an important source of error. The only disadvantage of this procedure is that the patient often remains drowsy for the rest of the day. In most cases heavy oral sedation is enough, but it is most important that the patient be really asleep; partial sedation may cause increased restlessness. *Richard de Alarcón*

ADRENAL GLANDS

1055. **Cushing's Syndrome with Bilateral Adrenal Hyperplasia: a Study of the Plasma 17-Hydroxycorticosteroids and the Response to ACTH**
M. M. GRUMBACH, A. M. BONGIOVANNI, W. R. EBERLEIN, J. J. VAN WYK, and L. WILKINS. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **96**, 116–125, March, 1955. 3 figs., 32 refs.

The difficulties of establishing a laboratory diagnosis of Cushing's syndrome are discussed. At the Johns Hopkins Hospital the authors determined the mean plasma levels of free and conjugated 17-hydroxycorticosteroids in 4 cases of Cushing's syndrome and compared them with those in 14 cases of the adrenogenital syndrome, in 4 of Addison's disease, and in a number of subjects with presumably normal adrenal function.

The mean plasma level of free corticoids in normal subjects was 8 μg. per 100 ml. and of the conjugated fraction 6·5 μg. per 100 ml. In the cases of Cushing's syndrome with adrenal hyperplasia the level of the free steroids was not always abnormally high, but when the conjugated fraction was determined in addition the total amount was always raised. In the cases of adrenogenital syndrome all values were low, and in those of Addison's disease no measurable corticoids could be detected After a 4-hour infusion of ACTH there was a substantially greater rise in the level of circulating corticoids in 2 of the patients with Cushing's syndrome associated with adrenal hyperplasia than in normal subjects or in the cases of adrenogenital syndrome; in the patients with Addison's disease there was no response at all to the infusion of ACTH. *B. Nordin*

1056. **Anticortisol Action of Aldosterone**
H. SELYE. *Science* [*Science*] **121**, 368–369, March 11, 1955. 7 refs.

The concept that the course of various biological phenomena, such as inflammation, is regulated by a balance between the opposing activities of two types of corticoid secreted by the adrenal cortex—the glucocorticoids and the mineralocorticoids—is an essential part of the theory of the general adaptation syndrome. However, there has hitherto been no direct proof that the adrenal cortex secretes effective quantities of any mineralocorticoid comparable to the synthetic substance deoxycortone. The recent isolation of aldosterone appeared to fill this gap, but it still remained to be determined whether aldosterone is actually an antagonist of glucocorticoids.

To this end experiments were carried out at the University of Montreal on 96 female rats which had undergone bilateral adrenalectomy. They were fed through-

out the experimental period on a standard diet without special salt supplements. Starting on the day of adrenalectomy, 400 μg. of cortisol (hydrocortisone) microcrystals and 20 μg. of aldosterone were injected daily into 10 rats, 6 received the aldosterone alone, 40 were given the cortisol alone, and 40 were given no treatment. For the quantitative assessment of inflammation "granuloma pouches" were prepared 48 hours later by the injection of 25 ml. of air under the dorsal skin followed immediately by the injection of 0·5 ml. of 1% croton oil into the air space. The surviving animals were killed on the 14th day after adrenalectomy. The mean gain or loss of weight, volume of inflammatory exudate, and weight of the spleen and thymus gland were determined and mortality calculated for each group. Under these conditions aldosterone diminished slightly but significantly the loss of weight and inhibition of formation of inflammatory exudate caused by cortisol, but did not significantly suppress the involution of the thymus and the spleen.

In a second experiment on 36 female rats (in which the "granuloma pouches" were prepared first, hormone treatment beginning 48 hours later simultaneously with bilateral adrenalectomy) the dose of aldosterone was increased to 25 μg. twice daily and additional control groups were treated with cholesterol and with deoxycortone acetate. In this dosage aldosterone was shown to be equally effective with deoxycortone in inhibiting the effects of cortisol, although in other respects the mineralocorticoid activity of aldosterone has been estimated to be 25 to 125 times greater than that of deoxycortone. Cholesterol had no inhibitory effect.

P. A. Nasmyth

1057. DCA-like Effects of Butazolidin in Normal Subjects and in a Patient with Addison's Disease

J. B. Gabriel, H. M. Katz, J. Reiman, and N. M. Luger. *Metabolism* [*Metabolism*] **4**, 119–128, March, 1955. 4 figs., 15 refs.

The effect of phenylbutazone ("butazolidin") on sodium and water metabolism was compared with that of deoxycortone acetate (DCA) in 3 healthy subjects with "minimum arthritic involvement" and one patient with Addison's disease at the Veterans Administration Hospital, Brooklyn, New York. A constant diet was given for a period of 6 days and a "half-aliquot of the daily diet" of each patient was analysed for the sodium and potassium content by the wet-ashing method of Wallace; the patient's plasma volume was determined by the use of azovan ("Evans") blue, and a Janke flame photometer was employed for estimating the plasma sodium and potassium levels.

Phenylbutazone was given in a dosage of 800 mg. daily for 6 to 12 days; this was followed by a rest period of 8 to 12 days and then DCA in oil in a daily dosage of 20 mg. was given intramuscularly for 4 to 8 days. In all 4 subjects administration of phenylbutazone was accompanied by sodium and water retention, this being most marked in the patient with Addison's disease. In the 3 healthy subjects sodium and water retention was similar in degree to that observed after administration of DCA. Phenylbutazone did not appear to have any effect on glucose metabolism, potassium excretion, or the eosinophil count.

The plasma volume increased in 2 of the healthy subjects by 7 and 12% respectively and in the patient with Addison's disease by 25%. The authors suggest that phenylbutazone by mouth may be a possible substitute for DCA in the treatment of Addison's disease.

I. McLean Baird

1058. Effect of Adrenaline on Adrenocortical Secretion

J. D. Hunter, R. I. S. Bayliss, and A. W. Steinbeck. *Lancet* [*Lancet*] **1**, 884–886, April 30, 1955. 1 fig., 19 refs.

In a study at the Postgraduate Medical School of London of the effect of adrenaline on adrenocortical activity the eosinopenia caused by adrenaline was compared with that caused by corticotrophin; the plasma levels of 17-hydroxycorticosteroids were also determined during the 30 minutes after subcutaneous injection of 0·3 to 0·5 mg. of adrenaline and during the 4 hours following intravenous injection of 30 units of corticotrophin. After the injection of adrenaline the eosinophil count fell by amounts ranging from 17 to 84% (mean 55%) of normal, the minimum being reached 2 to 4 hours after the injection. No consistent change in the plasma level of 17-hydroxycorticosteroids was observed. There was no consistent change in the eosinophil count in response to injection of saline solution in controls. When corticotrophin was injected the maximum fall in the eosinophil count occurred 3 to 4 hours afterwards, and the plasma level of 17-hydroxycorticosteroids rose consistently. The results showed that the eosinopenia caused by adrenaline is unrelated to a rise in the plasma level of 17-hydroxycorticosteroids. *P. A. Nasmyth*

DIABETES

1059. A Six-minute Test with Glucagon-free Insulin in the Classification of Diabetes and Prediabetes

G. E. Anderson. *Diabetes* [*Diabetes*] **3**, 462–465, Nov.–Dec., 1954. 3 figs., 4 refs.

At Brooklyn Hospital, Brooklyn, New York, the venous blood glucose level was determined at precisely 2, 4, and 6 minutes after the intravenous injection of 3 units of insulin free from glucagon (the hyperglycaemic-glycogenolytic factor) in 40 healthy subjects and 100 diabetic patients after a fast of 16 hours, previous studies having shown that the dominant change in blood glucose levels after the administration of insulin was well indicated in the first 6 minutes.

The results of the test were as follows. The non-diabetic control subjects showed a fall of 19% from the resting blood glucose level; in cases of the "juvenile" type of diabetes there was a rapid fall in blood glucose content, but in patients with a tendency towards obesity there was generally a poor response to insulin. The uncontrolled, obese-adult type of diabetic showed a poor response to insulin which improved with clinical treatment, while in the labile or "brittle" type of diabetic a

precipitous fall in blood glucose level occurred in 2 to 4 minutes, followed by a sharp rise within the 6-minute period.

The author suggests that the information obtained by this test " is sufficiently definitive and reproducible to serve as one means of classifying diabetics ".

F. W. Chattaway

1060. A Six-minute Test with Glucagon-free Insulin as a Guide to Treatment of Diabetes

G. E. ANDERSON and E. M. FRIBOURG. *Diabetes* [*Diabetes*] 3, 466–475, Nov.–Dec., 1954. 9 figs., 21 refs.

The response of the blood glucose level to the 6-minute test with glucagon-free insulin [see Abstract 1059] can be used as a guide to the efficacy of treatment of diabetes. The " juvenile " type of diabetic or well-controlled obese-adult diabetic shows a good response to insulin in this test. Any factor resulting in decreased control of the blood glucose content leads to a poor response to the test. It is claimed that the test serves as a more delicate index of clinical improvement or regression than does the casual determination of the blood glucose level.

F. W. Chattaway

1061. Experience with New Long-acting Insulins in Diabetes Mellitus in Childhood. (Erfahrungen mit neuen Verzögerungsinsulinen beim Diabetes mellitus im Kindesalter)

W. SWOBODA and E. ZWEYMÜLLER. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **85**, 231–237, March 5, 1955. 5 figs., 30 refs.

In this paper from the University Paediatric Clinic, Vienna, the authors describe their experience with the new long-acting (zinc suspension) insulins in the treatment of 30 diabetic children aged 3½ to 15 years. In all cases treatment was given in hospital, where the diet could be rigidly controlled and frequent blood sugar estimations carried out. The diet contained, per kg. body weight, 5 to 10 g. of carbohydrate (contributing approximately half the total calories), 2 g. of protein, and 2 to 3 g. of fat. The carbohydrates were fairly evenly distributed among the five meals of the day and the insulin was given at 6.30 a.m., that is, about three-quarters of an hour before the first meal.

In 9 children aged between 6 and 13 in whom the disease had been present only between 2 days and 7 months before admission the insulin requirements were initially established by the use of soluble insulin given first in three and then in two spaced doses daily, a slight reduction in the total dose being made before changing over to " insulin lente " (insulin zinc suspension). Good control was achieved in all cases and normal blood sugar curves were recorded on most occasions. On discharge from hospital the insulin dose was reduced to allow for the extra activity outside hospital, and during a follow-up period of from 4 to 16 months good control was considered to have been maintained in every case, the 24-hour urine specimens never containing more than 30 g. of sugar, and in 4 cases less than 10 g. It is pointed out, however, that a much longer period of observation is required before the ultimate value of these preparations can be established, since control of diabetes in recent cases is usually comparatively easy to achieve.

In 21 cases of longer standing (6 months to 9 years) treatment was changed from other types of insulin on account of poor control (10 cases), the inconvenience of the need for twice-daily injections (10 cases), and severe local reactions (one case). The results were considered good in 14 cases, moderate in 5, and poor in 2. In a number of cases in which the blood sugar curves were either of the Hallas-Møller Type A (high nocturnal and fasting blood sugar levels) or of Type C (high afternoon blood sugar values) attempts to produce a more normal curve were made by altering the proportion of amorphous to crystalline fractions, the ratio being 30 to 70 in the standard insulin zinc suspension. An increase of the amorphous fraction was successful in 5 cases showing a Type-C curve, but increasing the crystalline fraction in cases with a Type-A curve led to a more normal blood sugar curve in only 2. In 7 extremely labile cases some degree of stabilization was obtained with one or 2 daily injections of insulin zinc suspension, although wide variations in the blood sugar level persisted. In none of the 30 patients were sensitivity reactions observed, while hypoglycaemic attacks occurred in only one case and ketonuria in 2.

H. F. Reichenfeld

1062. Arteriosclerotic Heart Disease in Diabetes Mellitus. A Clinical Study of 383 Patients

I. M. LIEBOW, H. K. HELLERSTEIN, and M. MILLER. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 438–447, March, 1955. 8 figs., 44 refs.

The authors have investigated the prevalence of arteriosclerotic heart disease among 383 diabetic patients attending the out-patient departments of the University Hospitals of Cleveland, Ohio, the diagnosis in all cases being based on symptoms or abnormal findings indicating arteriosclerosis of the coronary arteries, thrombosis or occlusion of one or more coronary branches, sclerosis of a valve, and/or arteriosclerosis of the aorta. In this group of patients, of whom 73·6% were women and 26·4% men, clinical arteriosclerotic heart disease was diagnosed in 161 cases (42%), all in patients aged 40 or more. Aortic calcification was present in 126 cases (32·9% of the entire group) and showed about equal incidence in the two sexes. Angina of effort was present in 39 patients (10·2%), males and females again being about equally affected. The incidence of myocardial infarction, however, which was present in 6·8% of the patients, was three times higher among males.

The presence of arteriosclerotic heart disease was not related to the total serum cholesterol level, body weight, the degree of control of the diabetes or daily insulin dose, or to the duration of the disease; it was, however, positively related to sex, age, and the presence of hypertension.

James W. Brown

1063. Effect of Intravenously Administered Fructose on Blood Acid–Base Balance in Patients with Pre-existing Acidosis

O. R. KRUESI, M. F. GOODBODY, T. B. VAN ITALLIE, and J. G. HILTON. *Diabetes* [*Diabetes*] **4**, 104–106, March–April, 1955. 1 fig., 9 refs.

The Rheumatic Diseases

1064. **Response of Plasma 17-Hydroxycorticosteroids to Salicylate Administration in Normal Human Subjects**
A. K. Done, R. S. Ely, and V. C. Kelley. *Metabolism* [*Metabolism*] **4**, 129–142, March, 1955. 4 figs., bibliography.

Normal adult human subjects given salicylates in usual therapeutic doses failed to show consistent elevations in circulating levels of 17-hydroxycorticosteroids (17-OH-CS); indeed, these levels frequently were found to be reduced significantly. Salicylate administration was, in many cases, accompanied by greater fluctuations in plasma concentrations of these cortical steroids than were found as normal diurnal variations. Both increases and decreases in steroid concentrations were significantly greater on days of salicylate administration than on control days. The urinary excretion of 17-ketosteroids was unchanged, while significant reduction in the urinary output of 17-OH-CS was observed. These data suggest that, if increased adrenal steroid production follows salicylate administration, it is counter-balanced by an increased rate of removal of steroids from the circulation by a means other than urinary excretion.

There was no consistent correlation between eosinophil and steroid responses to salicylate.—[Authors' summary.]

1065. **Calcinosis and Collagen Diseases**
S. K. Conner. *Arizona Medicine* [*Ariz. Med.*] **12**, 277–280, July, 1955. 2 figs., 3 refs.

1066. **The Role of Peripheral Circulatory Disorders in Rheumatic Diseases.** (Die Rolle der peripheren Durchblutungsstörungen bei rheumatischen Erkrankungen)
M. Ratschow. *Zeitschrift für Rheumaforschung* [*Z. Rheumaforsch.*] **14**, 76–87, April, 1955. 26 refs.

At the Municipal Medical Clinic, Darmstadt, the oscillometric readings, pulse tracings, and angiograms obtained from groups of patients suffering from different rheumatic diseases gave comparable results and suggested that rheumatic disorders are frequently associated with arterial damage. This usually takes the form of constriction, which in the author's opinion is hardly likely to be of nervous origin and may be due to collagen changes. In such cases, also, capillary permeability, as tested by reactive hyperaemia, was shown to be altered, the difference between arterial and venous capillary pressures in rheumatic patients being largely abolished. The author believes that much of the traditional therapy of rheumatism is designed to increase peripheral blood flow, and the results of this study of 1,000 cases supports the view that vascular lesions do in fact exist in these disorders.

[The author includes among the variety of rheumatic diseases investigated cases of "muscular rheumatism", a diagnosis which apparently still has an appeal to German clinicians.] *David Preiskel*

1067. **The Radiological Diagnosis of Peripheral Circulatory Disorders in Rheumatic Diseases.** (Die Röntgendiagnostik peripherer Durchblutungsstörungen bei rheumatischen Erkrankungen)
A. Leb. *Zeitschrift für Rheumaforschung* [*Z. Rheumaforsch.*] **14**, 65–76, April, 1955. 7 figs.

In a study carried out at the Central Radiological Institute, Graz, of the changes in the peripheral circulation as a consequence of rheumatic disease a contrast medium was injected intra-arterially, and by taking serial radiographs it was possible to demonstrate peripheral vascular damage. In the normal hand the lateral and medial digital arteries are clearly defined, as is also the rich arterio-venous anastomotic network. But in cases of long-standing rheumatoid arthritis, for instance, narrowing or obliteration of the digital arteries at the level of the affected joints is usually found, while the terminal circulation is reduced owing to arterio-venous shunt, so that the venous return is retarded and varicosities appear. The author claims that by a modification of the radiological technique it is possible to demonstrate pathological changes in the peri-articular tissues.
David Preiskel

1068. **Corticotropin and Cortisone in Rheumatic Fever. Preliminary Report of the Effect on the Electrophoretic Patterns of Plasma or Serum Proteins of Children**
G. J. Van Leeuwen, H. G. Kelly, and R. L. Jackson. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **89**, 304–313, March, 1955. 5 figs., 29 refs.

Since the electrophoretic pattern of the plasma proteins is known to be abnormal in rheumatic fever and to return gradually to normal during recovery, the effect of treatment with corticotrophin (ACTH) or cortisone on the plasma proteins of 9 children with rheumatic fever was studied in the hope of elucidating the action of these drugs. In all, 24 specimens of plasma or serum were analysed, blood being taken in all cases on admission and again, if possible, 1½ to 3½ and 5 to 9 weeks later. The findings were compared with those previously obtained in 77 children with rheumatic fever not receiving hormone treatment.

The total protein level was not significantly affected by the treatment. In all but 2 cases the serum albumin level was decreased before treatment, as was also found in the control group, but in the treated cases the level rose rapidly and reached the normal range in 5 to 9 weeks, compared with an average of 4·2 months in the control group. Similarly the α-globulin level, which was consistently increased in the acute phase, returned to normal more rapidly in the treated group than in the controls, but the fall of the α_2-globulin level, which was similarly increased in the acute phase, was little affected by hormone therapy. The β-globulin level remained elevated or rose during hormone treatment, whereas in the controls

it showed no correlation with the activity of the disease. The γ-globulin level fell much more rapidly in patients receiving hormone treatment than in the controls.

It is suggested that these findings support the view "that the major effect of the hormones is related to hypersensitivity processes of the disease" and that they are therefore unlikely to prevent residual cardiac damage.

[It should be noted that the number of patients in this study and the number of observations made were small.]

C. Bruce Perry

1069. **The Mucoproteins in Rheumatic Fever in Infancy.** (Le mucoproteine nella malattia reumatica dell'infanzia) B. FANTUZZI and C. NEUHAUS. *Minerva pediatrica* [*Minerva pediat. (Torino)*] **7**, 478–481, April 14, 1955. 3 figs., 27 refs.

At the Paediatric Clinic, University of Milan, the authors determined the serum mucoprotein level in 8 normal children and in 13 suffering from rheumatic fever. They found that in the latter group the increased values for the serum mucoprotein content during the febrile period corresponded more closely to the clinical course of the illness than did the erythrocyte sedimentation rate. Thus its determination may be of value in diagnosis and prognosis.

L. Michaelis

CHRONIC RHEUMATISM

1070. **Rheumatoid Arthritis: Dye Retention Studies and Comparison of Dye and Radioactively Labelled Red Cell Methods for Measurement of Blood Volume**

A. ST. J. DIXON, S. RAMCHARAN, and M. W. ROPES. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 51–62, March, 1955. 3 figs., bibliography.

This report from the Massachusetts General Hospital (Harvard Medical School) and the Massachusetts Department of Public Health, Boston, describes investigations carried out on a statistical basis into the retention of dyes by patients with rheumatoid arthritis—a phenomenon similar to that observed in amyloidosis—and of its effect on the estimation of blood volume by dye-dilution methods. The authors had previously found that 114 out of 227 patients with rheumatoid arthritis gave a value for the retention of Congo red intermediate between those found in normal subjects and in cases of amyloid disease. In the present investigation estimates of the plasma volume as obtained by the dye-dilution method were compared with those obtained by an entirely different method utilizing radioactive sodium chromate (^{51}Cr), of which the technical details are given. The concentrations of both azovan ("Evans") blue and Congo red in plasma or serum at various times after injection were shown to lie on a straight line when plotted on semi-log. paper, showing that the loss of both dyes from the blood stream was exponential. Retropolation could therefore be employed in the calculation of plasma volume.

Investigations were carried out on 22 patients with various manifestations of the rheumatoid group of diseases and on 11 healthy control subjects. In the former the disease was of Grade II or III in severity (classification of the American Rheumatism Association) and of more than 5 years' duration. The results of blood-volume estimations by the azovan-blue method on the patients were within the same range as those on the normal subjects, whereas Congo red gave unexpectedly variable results which generally tended to be higher. Retention experiments showed that azovan blue disappeared from the circulation slightly, but significantly, faster in the rheumatoid subjects than in the controls. Congo red left the circulation of some patients at a rapid rate which could not be correlated with activity as indicated by the erythrocyte sedimentation rate, with blood volume, or with serum protein constitution. The loss into the synovial fluid of either dye was of only minor degree. No evidence of the saturation of tissues with Congo red after serial infusions could be obtained. The measurement of blood volume by means of erythrocytes labelled with ^{51}Cr gave consistently lower figures than the azovan-blue method.

The true blood volume was taken as the sum of the plasma volume estimated with azovan blue plus the erythrocyte mass estimated with ^{51}Cr. A statistical method was evolved whereby the mean blood volumes for the two groups were adjusted to the values they would have had if the groups had been of equal mean weight, and these values were compared in preference to values relating blood volume to unit weight or to unit surface area. By this method it was shown that the mean true blood volume of 10 women with rheumatoid arthritis was greater than that of 10 controls by 9·6%, a statistically significant difference, and that the plasma volume was 20·4% greater, although the erythrocyte mass was 7·1% less. The various possible causes for the rapid removal of Congo red in rheumatoid disease are reviewed, although no conclusions are reached, while other matters discussed include the differences between various authors' estimates of normal blood volume and the relation of the anaemia of rheumatoid arthritis to the increase in plasma volume. [The original paper should be consulted for technical details and for its extensive bibliography.]

Harry Coke

1071. **Nature of Anaemia in Rheumatoid Arthritis. I. Metabolism of Iron**

L. M. H. ROY, W. R. M. ALEXANDER, and J. J. R. DUTHIE. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 63–72, March, 1955. 5 figs., 28 refs.

In this paper from the University and the Rheumatic Unit, Northern General Hospital, Edinburgh, after a brief review of the literature on the type of hypochromic anaemia associated with rheumatoid arthritis and its mechanism of production the authors describe studies of iron metabolism carried out on 67 patients of both sexes suffering from rheumatoid arthritis. Samples of blood were collected in iron-free centrifuge tubes, sodium oxalate (1 mg. per ml.) being used as an anticoagulant when plasma was required, and the iron content estimated by Ramsay's method, modified by using sodium sulphite in place of hydroxylamine. The preparation of saccharated oxide of iron used was "iviron", a colloidal

solution containing 20 mg. of elemental iron per ml. Iron absorption was measured by giving 1·2 g. of ferrous sulphate at 10 a.m. and determining the plasma iron levels in blood samples taken at 10 a.m., 12 noon, and 2 and 4 p.m.

Serum iron levels before administration of the test dose ranged from 45 to 125 μg. (mean 87 μg.) per 100 ml. in the rheumatoid group as compared with 90 to 207 μg. (mean 158 μg.) in 70 normal control subjects. After giving 1·2 g. of ferrous sulphate the rise in serum iron level ranged from 42 to 202 μg. (mean 102 μg.) per 100 ml. in the rheumatoid group and from 72 to 185 μg. (mean 110 μg.) per 100 ml. in the controls. In one normal subject and one rheumatoid patient no rise in the serum iron content occurred. After the intravenous injection of 10 ml. of saccharated oxide of iron the injected iron was cleared from the plasma of patients with rheumatoid arthritis in 24 hours, whereas in normal subjects the clearance was not complete until 72 hours had elapsed. The concentration of iron was greater in the plasma than in the serum in all instances where the blood iron level exceeded 1,000 μg. per 100 ml., suggesting that below this critical level saccharated oxide of iron does not combine with fibrinogen.

It is concluded that the low blood iron level in patients with rheumatoid arthritis is not due to impaired absorption, and also that the rate of removal of iron from the plasma after intravenous injection of saccharated oxide of iron is more rapid in such patients than in non-rheumatoid subjects. Some evidence of transient impairment of liver function was found in some control subjects after the injection of saccharated oxide of iron, but not in the rheumatoid patients. The significance of these findings is discussed. *I. McLean Baird*

1072. **Amyloidosis in Rheumatoid Arthritis, and Significance of "Unexplained" Albuminuria. A Report of Eight Cases**

G. R. Fearnley and R. Lackner. *British Medical Journal* [*Brit. med. J.*] **1**, 1129–1132, May 7, 1955. 4 figs., 5 refs.

Cases of rheumatoid arthritis associated with amyloid disease are seen from time to time, but there is little information about the frequency of this serious complication. With this in mind the authors studied all the cases of rheumatoid arthritis seen by them in one year at the Postgraduate Medical School of London. These, numbering 183, were examined for the presence of albuminuria, regarded as being the most useful clinical pointer to possible amyloidosis. Persistent albuminuria was found in 24 cases, being without explanation in 12. Of these 12 patients, one died at an emergency operation and in 4 investigation was impossible. The remaining patients were investigated by Unger's modified Congo-red test or liver biopsy or by both methods, a positive result being obtained in all 7. Extensive amyloidosis was also found at necropsy in the fatal case referred to above.

That 8 cases were discovered among 183 patients with rheumatoid arthritis suggests that amyloidosis is not a rare complication of this condition. The duration of the arthritis in these 8 cases ranged from one to 18 years, but in 6 of the 8 patients it had been present for more than 10 years. Only one patient had clinical enlargement of both liver and spleen; 4 had hepatomegaly alone and 3 splenomegaly alone.

K. C. Robinson

1073. **Therapy of "Felty's Syndrome"**

P. Ellman, L. Cudkowicz, and J. S. Elwood. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 84–89, March, 1955. 3 figs., 23 refs.

In this paper from St. Stephen's Hospital, London, the authors describe 3 cases of Felty's syndrome and briefly discuss its pathogenesis. They consider that the granulocytopenia is probably due to hypersplenism, and postulate that it may be the end-result of reticulo-endothelial hyperplasia consequent upon a chronic inflammatory condition such as rheumatoid arthritis. In their opinion splenectomy is the treatment of choice for this syndrome, and other measures, such as the administration of haematinics, hormones, and blood transfusion, are of value only in making the patient fit for this operation. *J. Warwick Buckler*

1074. **Cardiac Changes in Rheumatoid Arthritis**

N. Egelius, O. Göhle, E. Jonsson, and F. Wahlgren. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 11–18, March, 1955. 33 refs.

In this report from Södersjukhuset, Stockholm, the authors add a further 13 cases of rheumatoid arthritis to the previous series of 288 cases reported by Jonsson *et al.* (in "Rheumatic Diseases," Philadelphia, 1952) in which a complete pathological examination of the heart was undertaken at necropsy. Previous reports are summarized and referred to in detail, and the authors observe that they show very varying results. In the present series of 13 cases, none showed any manifestation of rheumatic endocarditis. Healed or active pericarditis was found in 7 cases, and could be attributed in some of these to other concurrent diseases, but the authors conclude that there is some support for the occurrence of pericarditis as a manifestation of rheumatoid arthritis.

A further 100 clinical cases of rheumatoid arthritis were then examined and compared with the same number of controls, all cases of definite or suspected association with rheumatic fever being excluded, as were all cases in patients over 60 years of age and also cases in which there was other disease of the cardiovascular system. Examination was carried out by auscultation, phonocardiography, radiography, extensive electrocardiography, and by the hypoxaemia test. The summation of results showed that 8% of the rheumatoid group and 7% of the control group provided evidence of endocardial or myocardial abnormalities. The hypoxaemia test was, however, definitely positive in 8% of the rheumatoid group, but in only 4% of the control series. [This difference is not statistically significant.]

The authors emphasize that the absence of significant changes in the rheumatoid group was due to their care in the exclusion of all cases with a history of rheumatic fever. The finding of a positive hypoxaemia test is

thought to be due not to physical inactivation and probably not to anaemia, but perhaps to some vegetative vascular mechanism unconnected with any cardiac affection. *Harry Coke*

1075. **Treatment of Rheumatoid Arthritis by Prolonged Stimulation of the Adrenal Cortex**
H. F. West and G. R. Newns. *Lancet* [*Lancet*] **1**, 578–580, March 19, 1955. 4 refs.

The results of long-term treatment with corticotrophin, at the United Sheffield Hospitals, of 11 cases of rheumatoid arthritis are described and compared with those in a previously reported series (*Lancet*, 1953, **2**, 1123; *Abstracts of World Medicine*, 1954, **15**, 334) in which cortisone was used. In all 11 cases the disease was active and progressive and no improvement had been obtained with conservative treatment. The series consisted of 6 males aged 16 to 51 and 5 females aged 46 to 69. Treatment was maintained for from 12 to 24 months and is still being continued. The dosage of corticotrophin varied from 7½ to 40 units daily by intramuscular injection and was adjusted to produce a daily urinary output of 15 to 40 mg. of 17-ketogenic steroids. The only complications noted were pigmentation in 2 cases and a rise in diastolic blood pressure in 4 cases.

Comparison with the earlier series treated with cortisone acetate leads the authors to conclude that controlled administration of corticotrophin has produced better results so far. In particular, only 2 of the patients treated with corticotrophin showed any increase in bony erosion, whereas this occurred in 17 of the 27 cases treated with cortisone. Disadvantages of the treatment are said to be the need for daily injections (though these can be self-administered) and for frequent urinary assays. *Kathleen M. Lawther*

1076. **Joint Fluid Changes in Rheumatoid Arthritis**
W. D. Robinson, I. F. Duff, and E. M. Smith. *Journal of the Michigan State Medical Society* [*J. Mich. med. Soc.*] **54**, 270–291, March, 1955. 8 figs., 22 refs.

After a discussion of the characteristics of synovial fluid the authors describe a study carried out at the University of Michigan, Ann Arbor, of the changes in the joint fluid in rheumatoid arthritis following the systemic administration of cortisone and ACTH (corticotrophin) and also the intra-articular injection of hydrocortisone. Cell counts were made, the quality of the mucin clot formed on addition of acetic acid was observed, the relative viscosity was determined by means of an Ostwald viscosity pipette, and the polysaccharide concentration in the fluid was estimated by the method of Ragan and Meyers (*J. clin. Invest.*, 1949, **28**, 56; *Abstracts of World Medicine*, 1949, **6**, 351), with certain modifications. The authors confirmed a finding of Ragan and Meyers that there is a linear relationship between the concentration of polysaccharide in the synovial fluid and the logarithm of the viscosity of the fluid. Since the concentration of polysaccharide in rheumatoid joint fluid does not differ greatly from that in normal fluid whereas its viscosity is definitely less, it has been suggested that the polysaccharide in the fluid is poorly polymerized. The ratio of log. viscosity to polysaccharide concentration (the "polymerization index") is therefore considered to give a rough indication of the degree of polymerization of the polysaccharide in joint fluid.

In a number of patients with long-standing rheumatoid arthritis receiving ACTH, cortisone, or hydrocortisone systemically in high dosage the following changes in the joint fluid were observed: (1) a reduction in the cell count, especially affecting the polymorphonuclear leucocytes; (2) a change in the quality of the mucin clot in the direction of normal; (3) an increase in viscosity; and (4) an increase in the so-called "polymerization index". These effects were not observed when cortisone or hydrocortisone was given in doses under 100 mg. daily, and not in all cases receiving higher doses. The improvement in the characteristics of the joint fluid was rarely maintained with prolonged treatment. The same beneficial effects were noted in the fluid from 35 joints of patients receiving serial intra-articular injections of hydrocortisone. In a discussion of the use of intra-articular hydrocortisone in the treatment of rheumatoid arthritis the authors conclude that it may be of great value in selected cases. *C. E. Quin*

1077. **Ankylosing Spondylitis. A Review of 184 Cases**
F. D. Hart and N. F. Maclagan. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 77–83, March, 1955. 8 figs., 15 refs.

The authors review 184 cases (166 in males and 18 in females) of ankylosing spondylitis investigated at the Westminster Medical School, London. Symptoms were first noticed between the ages of 10 and 51 years in males and between 15 and 22 years in females. Low backache, low back stiffness with or without pain, and pain in the buttocks or thighs marked the onset of the disease in 135 patients (73·4%); in 24 (13%) the initial symptoms consisted of peripheral swellings and pain in the joints. Of the 184 cases, 43 at some time in the course of the disease developed peripheral arthritis, the knees being most commonly affected (28 cases), followed by the ankles (21 cases), feet (11 cases), wrists (11 cases), fingers (8 cases), and elbows (4 cases).

Attention is drawn to the occasional involvement of the sterno-manubrial joint, which may be tender on pressure or painful and swollen. Bony tenderness, commonly over the ischial tuberosities, pelvic brim, and greater trochanters, may occur and be associated with characteristic radiological appearances, which must be distinguished from those of bony tuberculosis. Iritis or iridocyclitis was observed in 25 cases (13·5%), iritis preceding the spondylitis in one case.

Spinal movements were measured with Dunham's spondylometer (*Brit. J. phys. Med.*, 1949, **12**, 126) before and after treatment with ACTH, cortisone, or deep *x*-ray therapy. In spite of the relief of pain following treatment, there was generally little improvement in spinal movement.

In several cases intercurrent disease was present, 7 patients having active pulmonary tuberculosis and 21 some evidence of peptic ulceration.

The serum protein level was estimated and flocculation tests performed in just under half the cases. These showed changes similar to those found in rheumatoid arthritis and severe prolonged infections, with low albumin, high globulin, and high fibrinogen values and a positive flocculation reaction in a proportion of cases.

J. Warwick Buckler

1078. **Psoriasis Spondylitica**

E. FLETCHER and F. C. ROSE. *Lancet* [*Lancet*] **1**, 695–696, April 2, 1955. 12 refs.

Among 100 consecutive cases of ankylosing spondylitis treated at the Royal Free Hospital, London, 4 cases were found in which psoriasis was also present. In view of the fact that the incidence of psoriasis in the general population is about 0·3%, the authors regard this finding as indicating the existence of an association between ankylosing spondylitis and psoriasis comparable to that known to exist between rheumatoid arthritis and psoriasis. The 4 cases are described in detail. Psoriasis developed before the ankylosing spondylitis in all of them. The spondylitis was clinically indistinguishable from the disease as it occurs without psoriasis. There was a family history of ankylosing spondylitis or psoriasis in 2 cases, one patient having 4 relatives with ankylosing spondylitis but none with psoriasis; the other 4 had relatives suffering from psoriasis but none from spondylitis. In view of reports that ulnar deviation and iritis do not occur in psoriasis arthropathica, it is of interest that one of the patients in the present series, who suffered from psoriasis and spondylitis with involvement of the peripheral joints, had both these complications.

The authors suggest that, by analogy with psoriasis arthropathica, the combination should be called psoriasis spondylitica.

C. E. Quin

1079. **Effect of Ankylosing Spondylitis on Ventilatory Function**

M. C. ROGAN, C. D. NEEDHAM, and I. MCDONALD. *Clinical Science* [*Clin. Sci.*] **14**, 91–96, Feb., 1955. 8 refs.

The ventilatory function of 35 patients of both sexes, ranging in age from 20 to 60 and suffering from ankylosing spondylitis but without cardio-pulmonary disease, was studied at Aberdeen Royal Infirmary before, during, and in 22 cases up to 18 months after, treatment by radiotherapy. Before treatment most of the patients showed low vital capacity and total lung volume, presumably due to the restricted movement of the chest, and the residual volume therefore constituted an abnormally high proportion of the total lung volume. This, however, did not signify the presence of emphysema, as was confirmed by the finding of a normal mixing efficiency. The maximum breathing capacity was not reduced in proportion to the vital capacity, presumably because these subjects have unusually free diaphragmatic movements and may thus achieve maximum breathing capacity by breathing at a more rapid rate than normal, though this was not measured on these subjects.

After radiotherapy there was no significant increase in total lung volume, but vital capacity and timed vital capacity increased, and residual volume decreased. The other indices of lung function all showed improvement, although the changes were not statistically significant for all tests. (There was no control group as the authors did not feel it was justifiable to withhold radiotherapy from any of these patients.)

W. A. Briscoe

GOUTY ARTHRITIS

1080. **Polycyclic Continuous Acute Gouty Arthritis. Long-term Clinical and Metabolic Study**

W. Q. WOLFSON. *Journal of the Michigan State Medical Society* [*J. Mich. med. Soc.*] **54**, 323–329, March, 1955. 2 figs., 4 refs.

The author describes the clinical and biochemical findings in a case of gout of unusual severity first seen in 1946 and kept under investigation at Wayne University College of Medicine, Detroit. The patient, a man aged 39 years, suffered from frequent attacks of acute gout, marked by intervening periods of only lessened intensity of the symptoms instead of the usual asymptomatic intervals. The case presented special difficulty because the patient was hypersensitive to colchicine. In addition there was at first a poor response to ACTH (corticotrophin) therapy, but this improved as treatment with this drug was continued. The urinary output of 17-ketosteroids was extremely low. The thyrotrophic, growth, and gonadotrophic functions of the pituitary gland appeared to be normal.

The slow appearance of increased adrenocortical function in spite of persistent stimulation with ACTH suggested the presence of selective hypopituitarism with respect to corticotrophin. This, it was thought, would explain the severity of the gout, since previous investigations have shown that increased endogenous secretion of corticotrophin will ultimately terminate severe attacks of gout. In the early stages of treatment it was found that no more than 0·36 mg. of colchicine daily could be tolerated without the development of toxic symptoms. Later, however, it was discovered that 0·42 mg. of colchicine daily could be given intravenously and this produced an appreciable reduction in the severity of the symptoms. The hypersensitivity to colchicine was abolished by ACTH therapy when this became available. Thereafter the combination of ACTH therapy with continuous colchicine administration in the maximum tolerated dosage enabled the acute manifestations of gout to be brought under control. Later the serum urate level was restored to normal with probenicid in a dose of 2 g. daily, 1 g. daily having proved insufficient for this purpose. The dull pain due to tophi was relieved by probenicid, but tended to recur when the drug was withdrawn. Old tophi did not disappear, but on the other hand no new ones formed during the 5-year period of study. Phenylbutazone was added to the therapeutic regimen in the hope of reducing the requirements of ACTH, and this was in fact achieved. In this case colchicine in the maximum dosage tolerated by the patient has been administered for 6 years, and ACTH therapy has been maintained for 4 years by means of careful adjustment of the dosage under strict observation.

C. E. Quin

Neurology and Neurosurgery

1081. **Urecholine in Myasthenia Gravis**
H. SCHWARZ. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **72**, 346–351, March 1, 1955. 7 refs.

The author has studied the effect of "urecholine" (urethane β-methylcholine chloride) on 10 patients suffering from myasthenia gravis. Previous treatment had consisted in the administration of neostigmine and ephedrine, and in 2 cases thymectomy was performed. The maintenance dose varied from 200 to 250 mg. daily [which is higher than would be tolerated by the average myasthenic patient].

Clinical improvement, most noticeable in the muscles innervated by the cranial nerves, occurred after a latent period of 3 to 14 days, and a reduction in the amount of neostigmine necessary was possible in 9 of the 10 cases treated, though in no case could administration of neostigmine be completely discontinued.

The author briefly considers the possible theoretical explanation for the improvement in muscular strength of patients with myasthenia gravis following the administration of choline esters. He suggests that the clinical findings, in particular the absence of any marked evidence of parasympathetic stimulation, support the theory that these choline esters are utilized in the elaboration of a precursor of acetylcholine from which acetylcholine is set free at the neuromuscular junction, and that a defect in acetylcholine function is probably a factor in myasthenia gravis. *Fergus R. Ferguson*

1082. **The Treatment of Tic Douloureux with Stilbamidine**
G. W. SMITH and J. M. MILLER. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **96**, 146–149, April, 1955. 15 refs.

Previous observation (*Ann. int. Med.*, 1953, **38**, 335) of the effectiveness of stilbamidine in the treatment of trigeminal neuralgia has encouraged the authors to give the drug a further trial in 16 cases of the disease at the Veterans Administration Hospital, Fort Howard, Maryland. In their experience stilbamidine, if properly administered, is an effective, safe, and inexpensive drug for this condition. Its only toxic effect is a late chronic neuropathy in the form of progressive sensory changes manifested by paraesthesiae usually confined to the face and appearing about 2 to 5 months after administration. Solutions are markedly affected by even short exposure to light, and must therefore be prepared immediately before administration. This is done by dissolving 0·15 g. of stilbamidine in 200 ml. of a 5% solution of glucose in distilled water. Administration is by intravenous infusion, which should be carried out slowly to avoid the transient shock-like reaction which may otherwise occur. The course of treatment consists in giving this amount once daily for 14 days.

The cycle of clinical events after the start of treatment is said to be characteristic. Patients noticed that the attacks of pain were less severe and less frequent from the 4th to the 8th day. Exacerbations of pain were, however, usually noted during the first month or two after the start of treatment. A gradual decrease in the severity and number of attacks followed. Complete freedom from pain occurred from 2 to 4 months after treatment.

Of the 16 cases, "excellent" results were claimed to have been obtained in 15, and a "good" result in one in which a second course of treatment was necessary.

[It will be interesting to see whether stilbamidine fulfils its early promise or whether, as with copper and vitamin B_{12}, further experience is disappointing.]

N. S. Alcock

DIAGNOSTIC METHODS

1083. **Paroxysmal Wave and Spike Activity and Diagnostic Sub-classification**
E. C. CLARK and J. R. KNOTT. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **7**, 161–164, May, 1955. 5 refs.

This paper from the State University of Iowa describes an attempt to determine the relationship between the type of spike-and-wave discharge, as defined by frequency, in the electroencephalogram of epileptic patients and the type of clinical attack and, more specifically, to answer the question whether spike-and-wave activity at 3 c.p.s. is diagnostic of petit mal.

The routine records of 178 patients at the Iowa Psychopathic Hospital were selected because they contained at least one spike-and-wave episode. Only 16% of these patients had uncomplicated petit mal and 22% major attacks only, the majority having more than one type of attack. Variations from the 3-c.p.s. pattern were commoner in those patients with mixed or major attacks, rates of 4 c.p.s. being particularly associated with the latter. When the fits had a supposed organic basis, 3-c.p.s. complexes were uncommon; on the other hand slow variants were equally common in patients with idiopathic and symptomatic attacks.

[Frequency is the simplest, but not the only, basis for the subdivision of spike-and-wave complexes. The authors fail to define what they mean by a "spike-and-wave" episode, and if this be thought unnecessary at this date, such sentences as "presumed organic etiology of seizures was found infrequently in those cases showing the classical 3 per sec. pattern" point the need. In the abstracter's experience 3-c.p.s. spike-and-wave, with onset, ending, form, and distribution such as may be seen during petit-mal attacks, has never been proved to be associated with organic cerebral disease.]

William Cobb

1084. **Changes in Electroencephalographic Reactivity, Disturbances of Symbolic Function, and Confusional States in Cases of Localized Disease of the Cerebral Hemispheres.** (Modifications de la réactivité EEG, troubles des fonctions symboliques et troubles confusionnels dans les lésions hémisphériques localisées)
J. BANCAUD, H. HECAEN, and G. C. LAIRY. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **7**, 179–192, May, 1955. 10 figs., 13 refs.

Failure of the alpha-rhythm blocking response, either unilateral or bilateral, has been generally attributed to the direct anatomical effects of cerebral lesions. The authors, however, in a study of 75 patients at the Hôpital Sainte-Anne, Paris, with lesions, mostly tumours, of one or both hemispheres, found that it is when there is " disturbance of symbolic function "—that is, aphasia, apraxia, or agnosia—that unilateral failure of the alpha-rhythm blocking response occurs, while bilateral failure is associated with mental confusion. The two effects may be observed during the course of a single illness, the time of their appearance corresponding with the patient's clinical state.

When the failure is partial, blocking may be made complete by reinforcing the stimulus with an additional task at the moment of opening the eyes, suggesting that the lesion has changed the threshold for this particular stimulus. In sleep the arousal responses are symmetrical, in contrast with what may be found with widespread massive destruction of a hemisphere. *William Cobb*

1085. **Electroencephalographic Rhythms from the Depths of the Frontal Lobe in 60 Psychotic Patients**
C. W. SEM-JACOBSEN, M. C. PETERSEN, J. A. LAZARTE, H. W. DODGE, and C. B. HOLMAN. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **7**, 193–210, May, 1955. 16 figs., 15 refs.

The electrical potentials recorded from multiple electrodes buried in the substance of the frontal lobes in 60 cases of psychosis studied at the Rochester (Minnesota) State Hospital are described in order to provide some sort of " baseline " for the study of such recordings. No claim is made for the normality or otherwise of the results. The recordings were mostly made as a preliminary to surgical treatment, usually leucotomy.

The technique involves the insertion through bifrontal burr-holes of fine, flexible, multicontact electrodes. Usually 6 to 8 electrodes, each with 6 contacts 1 cm. apart, were used. After insertion a period of up to 3 days was needed before the records became stable, after which they could be made as required up to as long as 6 weeks after insertion.

Consistent findings included alpha-like rhythms and fast (25-c.p.s.) rhythms, the latter from the lateral parts of the frontal lobes, while waves at 26 to 38 c.p.s. were recorded from the olfactory bulbs. Less commonly there were bilateral bursts of high-voltage waves at 2 to 5 c.p.s., not seen in scalp recordings. The effects of overbreathing, changes in blood sugar level, flicker, sleep, and anaesthesia were observed and are described.
William Cobb

BRAIN AND MENINGES

1086. **The Restoration of the Function of the Motor Analyser after Extensive Injuries to the Cerebral Hemispheres in Man.** (О восстановлении функции двигательного анализатора при обширных повреждениях больших полушарий головного мозга у человека)
V. M. UGRIUMOV and E. I. BABITCHENKO. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] **19**, 48–52, May–June, 1955. 2 figs., 9 refs.

The authors have studied the late results in 75 patients who had sustained severe injury of the cerebral hemispheres by gunshot wounds. They report that there was considerable improvement in motor function in many of these patients even after extensive unilateral damage to the frontal and parietal lobes. Of 15 of the patients who seemed to show full clinical recovery, however, myography revealed that some degree of depression of synaptic function was present in all. In 8 of them the deficiency was present not only on the previously paralysed side, but also, although to a lesser degree, on the opposite side. *L. Crome*

1087. **Prefrontal Leucotomy and the Anticipation of Pain**
A. ELITHORN, M. F. PIERCY, and M. A. CROSSKEY. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **18**, 34–43, Feb., 1955. 4 figs., 18 refs.

In order further to elucidate the changed attitude to pain following prefrontal leucotomy, the tolerance of pain and the autonomic reaction, in terms of change in electrical resistance of the palmar skin accompanying alteration in the rate of sweating, were measured in 14 patients at the National Hospital, Queen Square, London, the two stimuli employed being an electric shock and a red light which was regularly exhibited for a short interval 7 seconds before application of the electric stimulus. No emphasis was placed on absolute values, but only on the ratio between the response to the electric stimulus and the response to the warning red light. The method is described in detail. After the strength of the shock which the patient could just detect was established (perceptual level), the electric shock was then increased in strength by 2·5 volts on each occasion until the subject said " Stop ". This was the " refusal level ", and the ratio of this to the perceptual level was designated " pain tolerance ratio " (P.T.R.).

The results showed that the effects of prefrontal leucotomy on the patients' tolerance of this particular painful stimulus were very small and not significant, while the postoperative autonomic response to both the red light and the shock tended to be lower, but not significantly so. Determination of the expectancy ratio (that is, the ratio between mean response to the shock and mean response to the red light) revealed that postoperative values were with one exception all significantly higher ($p < 0.001$), thus showing that after leucotomy there is a reduction of autonomic disturbance (reflex sweating) following the threat of a painful stimulus, as compared with the autonomic disturbance which follows the painful stimulus itself.

A discussion of the findings of other workers regarding the effect of various psycho-surgical procedures on the perception of pain concludes: " these results are essentially in agreement with the present observations on the tolerance of a painful electrical stimulus—namely, that minor changes in pain tolerance cannot account for the relief of suffering which leucotomy often produces ". The authors conclude that 12 of the 14 patients examined showed postoperatively an increase in the ratio between the reaction to pain caused by a painful shock and that aroused by a preceding warning light, that is, a relative reduction in autonomic disturbance caused by the warning signal. This reduction in the anticipatory fear associated with a painful stimulus was not due to an alteration in the perception of pain or to a reduction in the amount of pain actually tolerated during the test.

John C. Kenna

1088. **Asymmetry of the Blood Pressure in Cases of Cerebral Tumour.** (Асимметрии артериального давления при опухолях головного мозга)
E. I. KANDEL. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] **19**, 14–20, May–June, 1955. 23 refs.

Working at the Institute of Neurosurgery, Moscow, the author investigated the presence of persistent asymmetry of blood pressure in 122 patients, 84 of whom had cerebral tumour and 28 localized inflammatory cerebral lesions. Asymmetry was considered to be present if the difference in pressure in the two brachial arteries was at least 10 mm. Hg.

Such stable asymmetry was found in 49 cases; in a further 3 it was intermittent, affecting the two sides alternately. Asymmetry was present in all of 21 cases with parietal location of the lesion, and in some in which the lesion was frontal. In view of this finding it is suggested that these areas of the cerebral cortex are involved in vasomotor regulation. Of 11 cases of tumour in the temporal lobe, there was only slight asymmetry in one. No asymmetry was observed in cases of lesion of the hypothalamic area, but because of its small size the hypothalamus was probably bilaterally involved in all of these cases. Lesions of the posterior fossa were frequently accompanied by asymmetry. There was, however, no correlation between the side of the raised blood pressure and that of the cerebral lesion.

L. Crome

1089. **Localization of Intracranial Lesions by Scanning with Positron-emitting Arsenic**
W. H. SWEET and G. L. BROWNELL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1183–1188, April 2, 1955. 9 figs., 14 refs.

The usual methods of measuring radiation as an aid to the diagnosis and location of intracranial tumours all suffer from the lack of resolution which is occasioned by the scatter of rays within the skull. In this paper from Harvard Medical School the authors explain how this can be partially overcome by the method of " coincidence counting ", which is based on the measurement of radiation (in the ordinary range of gamma rays) produced by the collision of positrons and electrons. The mass of the positron–electron pair appears as kinetic energy of two electromagnetic quanta which leave the site of the collision at an angle of 180 degrees to each other. Thus a pair of scintillation counters can be arranged, one on each side of the source, so as to register a count only when both photons resulting from the " annihilation " radiation strike the detectors. Single rays which are deflected and scattered are not registered.

In practice the method is as follows. The patient is given positron-emitting arsenic (^{74}As, which has a convenient half-life of 26 hours) in the form of 1 mg. of sodium arsenate and the apparatus is placed on each side of the patient's head so as to register the amount of radiation in the sagittal plane. Another circuit registers simultaneously the lateral asymmetry of the source of the radiation by means of a system containing a condenser which balances bilateral charges. If one of the detectors receives a greater number of impulses than the other this is reflected in a positive or negative charge in the condenser, and registered accordingly. The record is pictorial and its resolution is often very good. The procedure is painless and free from danger.

The authors report on the use of this method at Massachusetts General Hospital in 216 cases of cerebral lesions, including 126 in which the presence of a tumour had been verified by other means. Good correlation with the morphological findings was obtained for meningiomata, gliomata, and cerebral abscess. It is reckoned that the accuracy of the method is about 75% for tumours and 83% for abscesses. The " startling clarity " with which the lesions may be displayed is illustrated in reproductions of " positrocephalograms " which accompany the paper.

L. Crome

1090. **Studies in Cerebrovascular Disease. III. The Use of Anticoagulant Drugs in the Treatment of Insufficiency or Thrombosis within the Basilar Arterial System**
C. H. MILLIKAN, R. G. SIEKERT, and R. M. SHICK. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **30**, 116–126, March 23, 1955.

The authors describe the effects of anticoagulant therapy in 26 cases in which there were symptoms and signs of an insufficient blood supply through the basilar arterial system. The clinical picture in 5 cases was that of intermittent insufficiency of the basilar system, and in 21 that of occlusion of some part of the system. [The clinical features of both groups of cases have already been described (*Proc. Mayo Clin.*, 1955, **30**, 61 and 93).] The drugs given included heparin (for rapid action), ethyl biscoumacetate (" tromexan "), and dicoumarol, the dosage being adjusted to give a prothrombin time of 30 to 40 seconds (normal 18 to 20 seconds). Treatment was continued for as long as possible (often several months), but the authors admit that they have no evidence indicating the optimum duration of therapy. In all 5 cases in which there were episodes characteristic of intermittent insufficiency the attacks ceased during anticoagulant therapy. Of the 21 patients with clinical symptoms indicating complete occlusion of some part of the basilar system 3 died (14%); of the remainder, all except one improved markedly, though many had

residual neurological signs and symptoms. In contrast, the mortality in a group of untreated cases of basilar insufficiency or occlusion was 43%. The authors point out that in view of the potential danger of haemorrhage with anticoagulant therapy " such treatment should be reserved for specific categories of intracranial vascular disease ". They believe that it is indicated in intermittent insufficiency or occlusion within the basilar system and that it should be instituted as soon as the diagnosis has been established. *John N. Walton*

1091. **The Effect of Stellate Ganglion Block on Cerebral Circulation in Cerebrovascular Accidents.** [In English]
L. LINDÉN. *Acta medica Scandinavica* [*Acta med. scand.*] Suppl. 301, 1–110, 1955. 14 figs., bibliography.

1092. **Cerebral Cysticercosis. Common but Unfamiliar Manifestations**
E. R. BICKERSTAFF. *British Medical Journal* [*Brit. med. J.*] **1**, 1055–1058, April 30, 1955. 19 refs.

Attention is drawn to clinical manifestations other than epileptic convulsions which frequently occur in cerebral cysticercosis, and to the countries other than India where infestation is often acquired. Cases are described illustrating periods of disordered behaviour, transient pareses, intermittent obstructive hydrocephalus, dysequilibrium, meningo-encephalitis, involuntary movements, failing vision, and mental disturbances. Stress is laid on the cerebrovascular lesions, and on the importance of the posterior fossa forms of the disease.—[Author's summary.]

1093. **Pneumococcal Meningitis. A Short Survey of 78 Patients in the Bristol Clinical Area**
C. D. R. PENGELLY. *British Medical Journal* [*Brit. med. J.*] **1**, 870–874, April 9, 1955. 29 refs.

During the period January, 1946, to May, 1953, 78 cases of pneumococcal meningitis were admitted to hospitals for acute conditions in Bristol, 42 of the patients being under 10 years of age. Recurrences brought the total number of attacks to 84, in 82% of which the pneumococcus was cultured from the cerebrospinal fluid during life or at necropsy, and in the remainder from a stained smear. The commonest condition giving rise to the meningitis was middle-ear disease, although in nearly as many cases no predisposing cause was found.

Of the 78 patients, 38 died—a mortality of 49%. The highest mortality occurred in patients aged 50 or over. In 2 cases death occurred within 24 hours of the intrathecal injection in error of 500,000 units of penicillin. [This vital detail of therapeutics is not given sufficient prominence in teaching, and lethal intrathecal doses of penicillin continue to be administered.]

In most cases penicillin was given intrathecally (in doses of 5,000 to 30,000 units once or twice daily) and intramuscularly (100,000 to 1,000,000 units daily). Sulphonamides were usually given as well, and one or two additional antibiotics in some cases.

The author considers that the most effective treatment is probably daily intrathecal injection of 20,000 units of penicillin with 2,000,000 units intramuscularly for 7 to 10 days. He finds no evidence that any other antibiotic need be given; in fact the addition of chlortetracycline seems to worsen the prognosis. He suggests that it is probably wise nevertheless to give a sulphonamide by mouth in addition to the intrathecal and intramuscular injection of penicillin. *G. S. Crockett*

EPILEPSY

1094. **Drugs Used in Treatment of Patients with Petit Mal Epilepsy. A Serial Evaluation of New and Standard Drugs with Alternate Placebo Baselines in Identical Cases**
F. T. ZIMMERMAN and B. B. BURGEMEISTER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1194–1198, April 2, 1955. 3 refs.

In order to assess the relative value of drugs used in the treatment of petit mal the following five drugs were given to 72 patients at the Neurological Institute, Columbia University, New York: phenobarbitone, trimethadione (" tridione "), and 3 different succinimide compounds (" milontin ", PM 396, and PM 449). Each patient took all the drugs in rotation, with a placebo in the intervals between the different drugs, each of which was given for a period of 8 weeks; the duration of the whole trial was 2 years. Only 19 of the patients had " pure " petit mal, this condition being associated in the remainder with other forms of epilepsy. For the control of these other forms additional drugs were administered, but these were not taken into account for the purposes of the present study, the efficacy of the drug under test being assessed only on its action in reducing the number of attacks of petit mal.

The results were analysed statistically, and some of the conclusions are discussed. Trimethadione and one of the succinimide compounds, PM 396 (N-methyl-α:α-methylphenylsuccinimide) appeared to control petit mal more effectively than the other drugs. As the authors point out, however, all drugs were given in the same dose (0·3 g.) and it is therefore uncertain whether the other drugs might not have been more effective if given in larger doses. *L. Crome*

1095. **Treatment of Temporal-lobe Epilepsy by Temporal Lobectomy. A Survey of Findings and Results**
M. A. FALCONER, D. HILL, A. MEYER, W. MITCHELL, and D. A. POND. *Lancet* [*Lancet*] **1**, 827–835, April 23, 1955. 2 figs., 42 refs.

After a review of the historical background to epilepsy of temporal-lobe origin and of the various surgical procedures which have been used in treatment, the authors describe the findings and results in 30 patients treated by temporal lobectomy at the Maudsley Hospital, London. All the patients had seizures conforming to the various patterns of temporal-lobe epilepsy, and 12 were known to have had occasional grand mal also. All but one had personality disorder, while 28 of them showed an abnormal electroencephalographic focus in the temporal region, unilateral in 19, and with a predominance on one side in the remainder. Operation

consisted in excision of the temporal lobe including Ammon's horn and the uncus.

Pathological examination of the removed tissue showed small macroscopic lesions in 9 cases and less circumscribed microscopic changes in the remaining 21 cases. Follow-up examinations over a period of one to 4 years after operation showed that 12 patients had become free from fits and 14 others were greatly improved in regard to the number of fits, while 20 were benefited in respect of their personality changes, 17 markedly so. Such factors as age, sex, duration of symptoms, and laterality of a unilateral focus were without obvious influence on the postoperative results. The authors conclude that good results may be expected in any case of "psychomotor" epilepsy in which the focus is confined to one temporal lobe and major convulsive seizures have been absent or infrequent. Early surgical intervention should be considered if there is a likelihood of an underlying cerebral tumour or if the seizures prove disabling and resistant to medication, and also if a personality disorder develops. A plea is made for perseverance in this field of treatment of temporal-lobe epilepsy.

[The details of this important contribution should be examined in the original.] *J. B. Stanton*

1096. **Intellectual Changes following Temporal Lobectomy for Psychomotor Epilepsy. Preliminary Communication**

V. MEYER and A. J. YATES. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **18**, 44–52, Feb., 1955. 26 refs.

From the Institute of Psychiatry, Maudsley Hospital, London, the authors present preliminary findings on the intellectual changes occurring after temporal lobectomy in 18 patients with psychomotor epilepsy, who were selected for operation because of a single dominant focus in the anterior part of the temporal lobe and the occurrence of seizures which were not controlled by adequate anticonvulsant therapy. The patients' ages ranged from 15 to 48 years; in 11 cases the operation was on the dominant hemisphere, in 6 on the non-dominant hemisphere, and in one the dominance was doubtful. A number of tests, which are enumerated and described, were given before and after lobectomy with the intention of measuring changes in (*a*) intelligence, (*b*) learning, and (*c*) degree of retention of new knowledge. The tests were carried out 2 to 7 days before operation and 21 to 28 days after it. Results for all the tests are tabulated for each patient.

Preoperatively the intelligence test results showed a mean I.Q. for the group of 97·72 (range 67–120), performance I.Q. 97·88, and verbal I.Q. 94·38. Postoperatively, for the 9 patients subjected to operation on the dominant hemisphere, the mean I.Q. fell from 92·67 to 84·44 (significant at a level of 0·05), the mean performance I.Q. fell from 95·11 to 85·56 (significant at 0·05), and the mean verbal I.Q. fell from 91·78 to 85·33 (a difference just not significant). In this group of patients all subtest scores indicated a slight but consistent tendency to decline. These results and those obtained in the other tests are discussed and subjected to statistical analysis.

The authors conclude that the effects of temporal lobectomy on the intellectual function of patients with psychomotor epilepsy are as follows. "(1) General intelligence is relatively unimpaired. (2) Specific abilities may be impaired, at least for some time. (3) A significant learning disability may result. (4) The disability is strongly associated with lesions of the dominant hemisphere. (5) The disability may still be present a year after operation. (6) The learning disability is not a function of the level of intelligence of the patient or of intellectual changes following operation."

John C. Kenna

1097. **A Morphological Critique of Temporal Lobectomy**

L. CROME. *Lancet* [*Lancet*] **1**, 882–884, April 30, 1955. 5 refs.

The temporal lobes of 29 non-epileptic patients, 8 of whom were considered to be of normal intelligence and 21 were mental defectives, were examined at the Fountain Hospital, London. In all of them there were structural abnormalities of some degree—meningeal fibrosis, subpial gliosis, cortical atrophy, and gliosis of the white matter—but the changes were more marked in the mental defectives, 5 of whom had sclerosis of Ammon's horn. The brains of 61 mentally defective children with epilepsy were also examined. These showed similar though more intensive changes, with sclerosis of Ammon's horn in 9, but the changes were not limited to the temporal lobes.

In view of these findings the author doubts the significance of the changes, described by others as characteristic of temporal-lobe epilepsy and suggests that their importance may be slight. *L. G. Kiloh*

1098. **The Use of Phenylpropyl Allophanate (AC 148) in the Treatment of Epilepsy**

S. LIVINGSTON. *Journal of Pediatrics* [*J. Pediat.*] **46**, 394–397, April, 1955. 6 refs.

At the Johns Hopkins Hospital, Baltimore, 21 patients with idiopathic and 43 with organic epilepsy were treated for 6 to 18 months with phenylpropyl allophanate ("AC 148"), a new anticonvulsant drug. All of them had experienced daily or weekly seizures, 29 suffering from grand mal, 4 from petit mal, 8 from psychomotor attacks, 11 from akinetic or myoclonic spells, and 12 from mixed epilepsy. All had been receiving maximum doses of phenobarbitone, "mebaral", phenytoin, methoin, "paradione", or "tridione", alone or in combination, for at least one year. Most of the patients (52) were under the age of 14 years. The preparation was given in tablet form 2 or 3 times daily, the total daily dose varying from 750 mg. to 3 g.

The seizures ceased in 16 cases and were reduced in 10. Most of these good results were obtained in the cases of secondary epilepsy, only 3 of the cases of idiopathic epilepsy being benefited. No case of secondary epilepsy with psychomotor attacks improved. Side-effects consisted in drowsiness, dizziness, and a morbilliform rash (in one case). The author considers that, while AC 148 promises to be a useful drug in the treatment of epilepsy, a more extensive trial will be needed to substantiate its value and safety. *G. de M. Rudolf*

residual neurological signs and symptoms. In contrast, the mortality in a group of untreated cases of basilar insufficiency or occlusion was 43%. The authors point out that in view of the potential danger of haemorrhage with anticoagulant therapy " such treatment should be reserved for specific categories of intracranial vascular disease ". They believe that it is indicated in intermittent insufficiency or occlusion within the basilar system and that it should be instituted as soon as the diagnosis has been established. *John N. Walton*

1091. **The Effect of Stellate Ganglion Block on Cerebral Circulation in Cerebrovascular Accidents.** [In English]
L. LINDÉN. *Acta medica Scandinavica* [*Acta med. scand.*] Suppl. 301, 1–110, 1955. 14 figs., bibliography.

1092. **Cerebral Cysticercosis. Common but Unfamiliar Manifestations**
E. R. BICKERSTAFF. *British Medical Journal* [*Brit. med. J.*] **1**, 1055–1058, April 30, 1955. 19 refs.

Attention is drawn to clinical manifestations other than epileptic convulsions which frequently occur in cerebral cysticercosis, and to the countries other than India where infestation is often acquired. Cases are described illustrating periods of disordered behaviour, transient pareses, intermittent obstructive hydrocephalus, dysequilibrium, meningo-encephalitis, involuntary movements, failing vision, and mental disturbances. Stress is laid on the cerebrovascular lesions, and on the importance of the posterior fossa forms of the disease.—[Author's summary.]

1093. **Pneumococcal Meningitis. A Short Survey of 78 Patients in the Bristol Clinical Area**
C. D. R. PENGELLY. *British Medical Journal* [*Brit. med. J.*] **1**, 870–874, April 9, 1955. 29 refs.

During the period January, 1946, to May, 1953, 78 cases of pneumococcal meningitis were admitted to hospitals for acute conditions in Bristol, 42 of the patients being under 10 years of age. Recurrences brought the total number of attacks to 84, in 82% of which the pneumococcus was cultured from the cerebrospinal fluid during life or at necropsy, and in the remainder from a stained smear. The commonest condition giving rise to the meningitis was middle-ear disease, although in nearly as many cases no predisposing cause was found.

Of the 78 patients, 38 died—a mortality of 49%. The highest mortality occurred in patients aged 50 or over. In 2 cases death occurred within 24 hours of the intrathecal injection in error of 500,000 units of penicillin. [This vital detail of therapeutics is not given sufficient prominence in teaching, and lethal intrathecal doses of penicillin continue to be administered.]

In most cases penicillin was given intrathecally (in doses of 5,000 to 30,000 units once or twice daily) and intramuscularly (100,000 to 1,000,000 units daily). Sulphonamides were usually given as well, and one or two additional antibiotics in some cases.

The author considers that the most effective treatment is probably daily intrathecal injection of 20,000 units of penicillin with 2,000,000 units intramuscularly for 7 to 10 days. He finds no evidence that any other antibiotic need be given; in fact the addition of chlortetracycline seems to worsen the prognosis. He suggests that it is probably wise nevertheless to give a sulphonamide by mouth in addition to the intrathecal and intramuscular injection of penicillin. *G. S. Crockett*

EPILEPSY

1094. **Drugs Used in Treatment of Patients with Petit Mal Epilepsy. A Serial Evaluation of New and Standard Drugs with Alternate Placebo Baselines in Identical Cases**
F. T. ZIMMERMAN and B. B. BURGEMEISTER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1194–1198, April 2, 1955. 3 refs.

In order to assess the relative value of drugs used in the treatment of petit mal the following five drugs were given to 72 patients at the Neurological Institute, Columbia University, New York: phenobarbitone, trimethadione (" tridione "), and 3 different succinimide compounds (" milontin ", PM 396, and PM 449). Each patient took all the drugs in rotation, with a placebo in the intervals between the different drugs, each of which was given for a period of 8 weeks; the duration of the whole trial was 2 years. Only 19 of the patients had " pure " petit mal, this condition being associated in the remainder with other forms of epilepsy. For the control of these other forms additional drugs were administered, but these were not taken into account for the purposes of the present study, the efficacy of the drug under test being assessed only on its action in reducing the number of attacks of petit mal.

The results were analysed statistically, and some of the conclusions are discussed. Trimethadione and one of the succinimide compounds, PM 396 (N-methyl-α:α-methylphenylsuccinimide) appeared to control petit mal more effectively than the other drugs. As the authors point out, however, all drugs were given in the same dose (0·3 g.) and it is therefore uncertain whether the other drugs might not have been more effective if given in larger doses. *L. Crome*

1095. **Treatment of Temporal-lobe Epilepsy by Temporal Lobectomy. A Survey of Findings and Results**
M. A. FALCONER, D. HILL, A. MEYER, W. MITCHELL, and D. A. POND. *Lancet* [*Lancet*] **1**, 827–835, April 23, 1955. 2 figs., 42 refs.

After a review of the historical background to epilepsy of temporal-lobe origin and of the various surgical procedures which have been used in treatment, the authors describe the findings and results in 30 patients treated by temporal lobectomy at the Maudsley Hospital, London. All the patients had seizures conforming to the various patterns of temporal-lobe epilepsy, and 12 were known to have had occasional grand mal also. All but one had personality disorder, while 28 of them showed an abnormal electroencephalographic focus in the temporal region, unilateral in 19, and with a predominance on one side in the remainder. Operation

consisted in excision of the temporal lobe including Ammon's horn and the uncus.

Pathological examination of the removed tissue showed small macroscopic lesions in 9 cases and less circumscribed microscopic changes in the remaining 21 cases. Follow-up examinations over a period of one to 4 years after operation showed that 12 patients had become free from fits and 14 others were greatly improved in regard to the number of fits, while 20 were benefited in respect of their personality changes, 17 markedly so. Such factors as age, sex, duration of symptoms, and laterality of a unilateral focus were without obvious influence on the postoperative results. The authors conclude that good results may be expected in any case of "psychomotor" epilepsy in which the focus is confined to one temporal lobe and major convulsive seizures have been absent or infrequent. Early surgical intervention should be considered if there is a likelihood of an underlying cerebral tumour or if the seizures prove disabling and resistant to medication, and also if a personality disorder develops. A plea is made for perseverance in this field of treatment of temporal-lobe epilepsy.

[The details of this important contribution should be examined in the original.] *J. B. Stanton*

1096. **Intellectual Changes following Temporal Lobectomy for Psychomotor Epilepsy. Preliminary Communication**

V. MEYER and A. J. YATES. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **18**, 44–52, Feb., 1955. 26 refs.

From the Institute of Psychiatry, Maudsley Hospital, London, the authors present preliminary findings on the intellectual changes occurring after temporal lobectomy in 18 patients with psychomotor epilepsy, who were selected for operation because of a single dominant focus in the anterior part of the temporal lobe and the occurrence of seizures which were not controlled by adequate anticonvulsant therapy. The patients' ages ranged from 15 to 48 years; in 11 cases the operation was on the dominant hemisphere, in 6 on the non-dominant hemisphere, and in one the dominance was doubtful. A number of tests, which are enumerated and described, were given before and after lobectomy with the intention of measuring changes in (*a*) intelligence, (*b*) learning, and (*c*) degree of retention of new knowledge. The tests were carried out 2 to 7 days before operation and 21 to 28 days after it. Results for all the tests are tabulated for each patient.

Preoperatively the intelligence test results showed a mean I.Q. for the group of 97·72 (range 67–120), performance I.Q. 97·88, and verbal I.Q. 94·38. Postoperatively, for the 9 patients subjected to operation on the dominant hemisphere, the mean I.Q. fell from 92·67 to 84·44 (significant at a level of 0·05), the mean performance I.Q. fell from 95·11 to 85·56 (significant at 0 05), and the mean verbal I.Q. fell from 91·78 to 85·33 (a difference just not significant). In this group of patients all subtest scores indicated a slight but consistent tendency to decline. These results and those obtained in the other tests are discussed and subjected to statistical analysis.

The authors conclude that the effects of temporal lobectomy on the intellectual function of patients with psychomotor epilepsy are as follows. "(1) General intelligence is relatively unimpaired. (2) Specific abilities may be impaired, at least for some time. (3) A significant learning disability may result. (4) The disability is strongly associated with lesions of the dominant hemisphere. (5) The disability may still be present a year after operation. (6) The learning disability is not a function of the level of intelligence of the patient or of intellectual changes following operation."

John C. Kenna

1097. **A Morphological Critique of Temporal Lobectomy**

L. CROME. *Lancet* [*Lancet*] **1**, 882–884, April 30, 1955. 5 refs.

The temporal lobes of 29 non-epileptic patients, 8 of whom were considered to be of normal intelligence and 21 were mental defectives, were examined at the Fountain Hospital, London. In all of them there were structural abnormalities of some degree—meningeal fibrosis, subpial gliosis, cortical atrophy, and gliosis of the white matter—but the changes were more marked in the mental defectives, 5 of whom had sclerosis of Ammon's horn. The brains of 61 mentally defective children with epilepsy were also examined. These showed similar though more intensive changes, with sclerosis of Ammon's horn in 9, but the changes were not limited to the temporal lobes.

In view of these findings the author doubts the significance of the changes, described by others as characteristic of temporal-lobe epilepsy and suggests that their importance may be slight. *L. G. Kiloh*

1098. **The Use of Phenylpropyl Allophanate (AC 148) in the Treatment of Epilepsy**

S. LIVINGSTON. *Journal of Pediatrics* [*J. Pediat.*] **46**, 394–397, April, 1955. 6 refs.

At the Johns Hopkins Hospital, Baltimore, 21 patients with idiopathic and 43 with organic epilepsy were treated for 6 to 18 months with phenylpropyl allophanate ("AC 148"), a new anticonvulsant drug. All of them had experienced daily or weekly seizures, 29 suffering from grand mal, 4 from petit mal, 8 from psychomotor attacks, 11 from akinetic or myoclonic spells, and 12 from mixed epilepsy. All had been receiving maximum doses of phenobarbitone, "mebaral", phenytoin, methoin, "paradione", or "tridione", alone or in combination, for at least one year. Most of the patients (52) were under the age of 14 years. The preparation was given in tablet form 2 or 3 times daily, the total daily dose varying from 750 mg. to 3 g.

The seizures ceased in 16 cases and were reduced in 10. Most of these good results were obtained in the cases of secondary epilepsy, only 3 of the cases of idiopathic epilepsy being benefited. No case of secondary epilepsy with psychomotor attacks improved. Side-effects consisted in drowsiness, dizziness, and a morbilliform rash (in one case). The author considers that, while AC 148 promises to be a useful drug in the treatment of epilepsy, a more extensive trial will be needed to substantiate its value and safety. *G. de M. Rudolf*

Psychiatry

1099. **The Cerebral Representation of the Median Plane of the Body Image and Visual Space.** (Über die zerebrale Vertretung der Mediane von Körperbild und Sehraum)
H. HOFF and O. PÖTZL. *Wiener Zeitschrift für Nervenheilkunde* [*Wien. Z. Nervenheilk.*] **11**, 12–42, 1955. 24 refs.

The median plane separating the two symmetrical halves of the body is normally only an idea—a " plane of reference ". In certain cases, however, it is perceived, felt, or seen, or at any rate has sensory qualities. According to the authors, this is due to inadequate integration of the two halves of the body image or of perception of the right and left sides of the outside world. The process of integration normally takes place in the thalamus or, for lower neurone perceptions, in the spinal cord. The authors believe they can identify certain pathways with this process. If they are interfered with by a lesion, the patient becomes aware of the median plane or perception around the midline becomes distorted. If the integration of the two halves is disturbed in time, a peculiar sensation of slowing-down or speeding-up of certain movements occurs.

[This paper is a typical example of the work of the former Vienna school, involved theories borrowed from biophysics and electrophysiology being supported by observations on one or two relatively rare cases of disturbed brain function due to localized lesions. It is, however, highly stimulating, in spite of the disproportion between ideas and interpretations and observed facts.]

W. Mayer-Gross

1100. **On Disturbances of Imagery. (A Contribution to the Psychopathology of the Frontal Lobes.)** (Über Störungen der Vorstellungsfähigkeit. (Ein Beitrag zur Psychopathologie des Stirnhirns))
W. KLAGES. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **193**, 243–251, 1955. 35 refs.

The author has investigated imagery at the University Neurological Clinic, Tübingen, in 20 cases of brain injury, tumour, or circumscribed atrophy of various parts of the brain. He found a disturbance of the ability to imagine, or a characteristic lack of persistence and stability of images in patients in whom the convexity of the frontal lobes was damaged. All sensory fields were tested, the patient being asked to imagine such things as a red apple, a horse, the noise of a railway engine or an alarm clock, or a painful blister on the thigh. The author relates failure in these tests to a number of well-known frontal-lobe symptoms, such as the short-circuited thinking and acting, lack of foresight, and disturbances of productivity in thinking, of fantasy, and of evaluation. [It would certainly be worth while to apply similar tests to patients who have undergone prefrontal leucotomy.] *W. Mayer-Gross*

ALCOHOLISM AND DRUG ADDICTION

1101. **A Medico-social Study and Therapeutic Assessment of 225 Cases of Alcoholism Treated with Disulfiram.** (Etude médico-sociale et bilan thérapeutique de 225 cures de désintoxication alcoolique par le tétra-éthyl-thiourame disulfure)
P. DELORE, —. GUICHARDIERE, R. LAMBERT, and J. FONTVIEILLE. *Presse médicale* [*Presse méd.*] **63**, 569–571, April 20, 1955. 15 refs.

The authors of this paper suggest that reported cure rates among alcoholics treated with tetraethylthiuram disulphide (disulfiram; " antabuse ") of 50% or more are prematurely optimistic. In the series of 225 cases here described from the University of Lyons long-term cure was achieved in only 33%. The authors have found that the longer and more thorough the follow-up, the more it becomes apparent that even those patients who have responded most favourably to treatment may eventually relapse. Nevertheless, they believe that this method of treatment, although only one element in the struggle against alcoholism, is of great value and has far-reaching possibilities, especially when supported by appropriate adjuvant measures.

In reviewing the essentials of the technique they stress the importance of a full preliminary examination, medical, psychiatric, and ophthalmological. It is important that the patient should not be treated as an evil-doer, especially if he has undertaken to accept treatment as the result of legal proceedings following a breach of the law. Small initial doses of disulfiram are advocated—of the order of 1 g. only. Alcohol is best given intravenously, the dose being reduced when evidence of distress becomes apparent. Careful observations are recorded of the alcohol–disulfiram reactions, with particular regard to the cardiovascular system. Tachycardia is almost the rule and a fall in blood pressure, sometimes profound, is extremely common. Nevertheless, the authors have never encountered a case of death attributable to the use of disulfiram. In 5 of their cases the usual technique was modified to include a preliminary period of withdrawal therapy lasting for 5 days, during which gradually diminishing doses of alcohol were given intravenously. This was followed by 5 days of " disgust-therapy ", apomorphine and wine being given twice daily, after which disulfiram was administered in reduced doses. Although few patients were so treated, it is believed that this modified technique has certain special merits.

The results of treatment of alcoholism are difficult to interpret, because the criteria of cure are at best arbitrary and because relapses occur so unpredictably that a proper follow-up study should extend over very many years. However, 74 (33%) of the authors' 225 patients remained completely abstemious for long enough to be classified as " outcome very satisfactory ". In 54 cases

(24%) the outcome was "doubtful"; some of these patients had not maintained complete abstention, some were believed, despite their denials, to have begun drinking again, while others failed to return for follow-up. It is not impossible that some of these doubtful cases have in fact been cured, in which case the estimated cure rate of 33% may be too low. In as many as 97 cases (43%), however, the outcome was frankly poor. The authors point out that successful results were commonest in those who had succeeded in forsaking bad company, who had understanding wives and a sense of responsibility towards them and their children, or who had initially begun drinking as an escape from grief. Poor results were found most often among those who lived alone, those who had fallen into the company of alcoholics, those who had become addicted to alcohol soon after the age of adolescence, or those who were frankly psychopathic.

It is concluded that to be effective, disulfiram therapy must be supported and followed by appropriate psychotherapy in the widest sense, in which wives, friends, and reputable organizations have a vital part to play if relapse is to be avoided. *Adrian V. Adams*

1102. **Chlorpromazine in the Treatment of Acute Alcoholism**

E. H. MITCHELL. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 363–367, April, 1955. 4 figs.

The results of the treatment of 156 alcoholic patients with chlorpromazine (Group 1) are compared with those in 150 patients of comparable age, sex, and with similar clinical features who were treated with barbiturates and mephenesin (Group 2). Those in Group 1 received 50 mg. of chlorpromazine intramuscularly or intravenously on admission and 50 to 100 mg., according to body weight, orally every 4 hours thereafter; in Group 2 each patient received 250 mg. of quinalbarbitone intravenously, and 60 mg. of butobarbitone with 100 mg. [given elsewhere in the paper as 1·5 g.] of mephenesin every 3 hours until bedtime. Both groups were given intravenously 1,000 to 1,500 ml. of 5% glucose in saline to which was added vitamin-B complex and vitamin C, administration of the vitamins being repeated (intramuscularly) daily in all cases. At bedtime, one to 1·5 g. of chloral hydrate was given to all patients in Group 2 and to such in Group 1 as were still awake. The doses of all drugs were progressively diminished so that patients on discharge were receiving the vitamins only. A minimum of 5 days' treatment was aimed at, although patients were free to leave the sanatorium at any time.

Of the patients in Group 1, 33 (21%) showed a mild postural hypotension, and a further 7, all receiving 100 mg. of chlorpromazine, showed severe hypotension with syncope, but on reduction of the dose to 25 or 50 mg. no further difficulty was encountered. One poor-risk patient with cardiac and hepatic disease died. Tachycardia was noted in 11%, and 3 patients in this group developed delirium tremens. On the credit side the outstanding result of chlorpromazine therapy was the ease with which patients became relaxed and their amenability to suggestion; they took solid food earlier than patients in Group 2 and could often be discharged 24 hours in advance of the latter. In patients in Group 2 sedation was slower, nausea and vomiting rather more persistent, and there were disturbances in equilibrium accompanied by frequent falls.

The author concludes that, on the whole, chlorpromazine appears to be the more useful form of therapy in acute alcoholism. *R. J. Matthews*

1103. **Use of Chlorpromazine in the Withdrawal of Addicting Drugs. Preliminary Report**

C. E. FRIEDGOOD and C. B. RIPSTEIN. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 230–233, Feb. 10, 1955. 17 refs.

Chlorpromazine, an autonomic nervous system depressant, was tried at Maimonides Hospital, Brooklyn, New York, in the treatment of 8 patients suffering from drug addiction (5 to morphine, 2 to pethidine ("demerol"), and one to pentobarbitone), the duration of addiction varying from 6 months to 5 years. The drugs of addiction were abruptly and completely withdrawn, and chlorpromazine was given parenterally in a dosage up to 600 mg. daily for 2 or 3 days, followed by 200 mg. daily by mouth. When the patients were discharged they were maintained on 25 to 50 mg. by mouth three times a day. No withdrawal symptoms were observed; the patients slept and ate well and were relaxed, calm, and cooperative. One addict with a chronic peptic ulcer underwent subtotal gastrectomy on the eighth day; recovery was uneventful. Another patient with secondary bone carcinoma has been maintained for 8 months on 75 mg. of chlorpromazine daily. *A. C. Tait*

TREATMENT

1104. **Chlorpromazine in Treatment of Elderly Psychotic Women**

C. P. SEAGER. *British Medical Journal* [*Brit. med. J.*] **1**, 882–885, April 9, 1955. 7 refs.

Chlorpromazine was tried at Bristol Mental Hospitals in the treatment of 48 women aged 58 to 87 whose mental state varied but who all constituted a nursing problem, being noisy, abusive, violent, destructive, and requiring constant attention for feeding and dressing. One group of 11 patients received 50 mg. of chlorpromazine by injection three times a day for one week, followed by 50 mg. by mouth three times a day for 3 weeks. A second group of 13 patients were given 25 mg. by mouth thrice daily for 3 days, increased to 50 mg. for 10 days, and then to 75 mg. for 2 weeks. An equal number of patients in each group served as controls, receiving injections or tablets of an inert substance. At the end of 4 weeks the treated and control groups were reversed, so that the treated patients received the inert substance and the previous controls received chlorpromazine.

In the first 4-week period all 11 patients given chlorpromazine by injection and by mouth improved, as did one of the controls. In the second 4-week period 3 of the control (but previously treated) patients improved,

while 7 of the treated (previously control) patients did so. Of the 13 patients given chlorpromazine by mouth only, 2 had to be withdrawn from the trial, and of the remainder 7 improved in the first 4 weeks as did 5 of the 13 controls; in the second 4 weeks 3 of the control (previously treated) patients and 12 of the treated (previously control) patients improved. Altogether 33 patients responded to the drug.

During treatment the patients looked ill, with pinched, drawn faces and pallor, although there were no subjective complaints. Pyrexia and tachycardia were more frequent in the patients receiving the drug by injection, temperature rising to 103° F. (39·4° C.) in 9. Drowsiness and giddiness occurred in 11, and jaundice, dryness of the mouth, abdominal pain, diarrhoea, polyuria, and rashes were also observed. No patient became fit for discharge, but 2 were able to have week-end leave and several became employable. Improvement lasted for 2 to 6 weeks after withdrawal of the drug, thus making periodic courses possible in place of continuous sedative treatment. The author advises rest in bed for 1 to 2 hours after administration of chlorpromazine to lessen the risk of fracture in these elderly patients. He has found that the restlessness following fracture can be readily controlled by intramuscular injection of the drug.

G. de M. Rudolf

1105. **Chlorpromazine in Obsessive-compulsive and Allied Disorders**

W. H. Trethowan and P. A. L. Scott. *Lancet* [*Lancet*] 1, 781–785, April 16, 1955. 15 refs.

At Manchester Royal Infirmary 59 psychoneurotic out-patients showing obsessive or compulsive symptoms were selected for a therapeutic trial of chlorpromazine. Their average age was 35, and symptoms had been present in most cases for many years, in 27 since childhood or adolescence. Six of the patients exhibited a classic obsessive-compulsive neurosis, while the remainder showed mixed conditions of aggression, phobias, anxiety and tension, depression, and some somatic symptoms with obsessive-compulsive features; 45 of them were moderately incapacitated. The patients were arbitrarily divided into 4 groups and given one of the following courses of treatment: (1) chlorpromazine for 4 to 5 weeks, a placebo for 1 to 3 weeks, and again chlorpromazine for 2 to 3 weeks; (2) chlorpromazine for 4 to 6 weeks, a placebo for 1 to 2 weeks, and no treatment for 1 week; (3) a placebo for 2 to 3 weeks, chlorpromazine for 4 to 6 weeks, and again the placebo for 1 to 3 weeks; and (4) a placebo for 2 to 3 weeks, chlorpromazine for 4 to 7 weeks, and no treatment for 1 week. The daily dosage of chlorpromazine was 50 to 75 mg. for the first week and 150 to 200 mg. thereafter. The patients were interviewed separately at each attendance by each of the two investigators, only one of whom knew what treatment the patient was having.

A total of 27 patients (46%) showed a significant response to the first course of chlorpromazine, but relapsed when it was withdrawn after 4 to 6 weeks, 6 of them becoming much worse than before treatment. When chlorpromazine was given again none responded as well as on the first occasion, and 10 did not respond at all. Of the 32 patients who did not respond to the drug, 20 were unchanged, 2 became worse, and 10 showed some improvement whatever treatment was given.

The symptoms which responded significantly to the administration of chlorpromazine were anorexia, anxiety, tension, hypochondria, aggressive impulses, lack of concentration, and insomnia. In some cases a gain in weight and a transient fall in blood pressure (average 19 mm. Hg) were observed. The side-effects of the drug included jaundice, short attacks of pyrexia, hypnagogic hallucinations, rashes, dizziness, thirst, abdominal discomfort, constipation, and drowsiness. Jaundice occurred in 3 patients after only 9, 18, and 19 days respectively of treatment and lasted about 3 weeks; contact with a case of infective hepatitis had occurred in one case. The authors conclude that better results might have been obtained had chlorpromazine been withdrawn less suddenly, that the drug is of value in controlling certain symptoms in obsessive-compulsive disorders, and that it can safely be given to out-patients under adequate supervision.

Elizabeth M. Watkins

1106. **Reserpine in Treatment of Chronic Psychotics. Preliminary Observations**

E. S. Foote. *British Medical Journal* [*Brit. med. J.*] 1, 1192–1193, May 14, 1955. 2 refs.

At Herrison Hospital, Dorchester, reserpine was tried in the treatment of 32 chronic psychotic patients, including 26 schizophrenics, who presented behaviour problems, including destructiveness, faulty habits, and impulsive violence; none could be employed in any way. Initially, 6 patients received 1 mg. of reserpine 4 times a day, but in view of the hypotensive effects of this dosage it was decided to try 0·5 mg. three times a day. The dosage was constantly under review, and it was found that the effective dosage varied from 0·5 mg. to 1 mg. 4 times daily. In only 5 patients was there no improvement in behaviour in response to treatment; in most of the remaining patients improvement was noted between the first and second weeks, but in some it was observed at once (within 3 days) and in a few only after 3 months' treatment. The drug had the most marked effect on the patients with destructive impulses and dirty habits; they became quiet and cooperative, fed themselves, and often helped each other; 20 of the 32 regularly attended occupational therapy classes. Side-effects included slight drowsiness (easily controlled by small doses of amphetamine), transient looseness of the bowels, and stuffiness of the nose. Oedema developed in 3 patients, but the mechanism of this could not be determined in spite of careful investigation.

The author suggests that in view of the promising results in this small series an intensive trial of reserpine in the treatment of psychotic patients should be carried out.

E. H. Johnson

1107. **Reserpine in the Treatment of Anxious and Depressed Patients**

D. L. Davies and M. Shepherd. *Lancet* [*Lancet*] 2, 117–120, July 16, 1955. 5 refs.

Dermatology

1108. **Hidradenitis Suppurativa of the Adult and its Management**
K. STEINER and L. D. GRAYSON. *Archives of Dermatology* [*Arch. Derm.* (*Chicago*)] **71**, 205–211, Feb., 1955. 2 figs., 25 refs.

The aetiology, pathogenesis, and management of hidradenitis suppurativa are discussed and 45 cases (23 acute and 22 chronic), seen at the Veterans Administration Hospital, Brooklyn, New York, are reviewed. In about half of the acute cases some form of mechanical irritation such as friction, pressure, or shaving of the axillae preceded the onset of the hidradenitis, but factors of this kind played little part in the chronic cases. In contrast, systemic disorders, which included diabetes, obesity, virilism, and low urinary excretion of 17-ketosteroids, characterized 18 of the chronic cases, while acne was common, being severe in 9 of the 12 patients with chronic generalized hidradenitis. A haemolytic *Staphylococcus aureus* was usually cultured from acute lesions, but the organisms isolated from chronic lesions were in general secondary invaders, primarily non-pathogenic.

The acute form of the disease responded to simple measures, including administration of antibiotics, incision, and drainage; there were no recurrences. In the chronic form, however, intensive antibiotic therapy and irradiation, combined with a careful management of systemic disorders, were necessary to obtain even temporary healing, and the over-all results over a period of years were discouragingly poor. In 6 cases of chronic generalized hidradenitis radical excision with subsequent grafting resulted in cure, and the authors believe that this is the only form of treatment which offers any hope of success in an otherwise incurable disease.

E. W. Prosser Thomas

1109. **Favus: a Report of Seven Related Cases**
J. HANSELL and B. M. PARTRIDGE. *British Medical Journal* [*Brit. med. J.*] **1**, 1510–1511, June 25, 1955. 2 figs., 3 refs.

1110. **The Area Factor in the Irradiation Therapy of Warts**
R. G. PARK. *British Journal of Dermatology* [*Brit. J. Derm.*] **67**, 98–100, March, 1955. 4 refs.

The author briefly describes the variation in the biological response to irradiation that occurs with change in field size, with particular reference to the treatment of warts by contact *x* rays. The lack of success with the standard "dermatological" dose in the treatment of warts is discussed, and it is suggested that the erythema doses recommended should be corrected—that is, they should be increased for small lesions.

At Wellington Hospital, New Zealand, a series of 30 patients with common warts were given irradiation therapy, 15 receiving the standard textbook treatment and 15 receiving an intensified dosage of *x* rays within the limits of safety. The warts disappeared in one-third of the cases given the standard dosage and in two-thirds of those given the increased dosage. Since it has been suggested that any success from irradiation therapy of warts is due to its psychological effect, a further group of 15 patients received no effective irradiation; it was found that the warts disappeared in only 4 of the cases in this group. There were no untoward radiation effects at the site of the warts which responded to treatment.

R. D. S. Rhys-Lewis

1111. **Local Action of Heparin on Xanthomas**
T. CORNBLEET. *Archives of Dermatology* [*Arch. Derm.* (*Chicago*)] **71**, 172–176, Feb., 1955. 5 figs., 9 refs.

Heparin appears to induce the elaboration in plasma of an agent capable of modifying lipoprotein particles, and the present investigation, undertaken at the Cook County Hospital, Chicago, is reported not so much as a practical method of treatment but as a contribution to the further understanding of the xanthomatous process. Heparin was injected into xanthomata in 8 patients, the drug being deposited within and under the lesions. After an average of 12 to 15 injections, each of 5,000 units of heparin, at weekly or twice-weekly intervals, the majority of the xanthomata flattened and disappeared. Prothrombin time was determined before and after the first injection. Lesions injected with water or saline did not involute, but the author recognizes that further investigation is necessary to be certain that pressure *per se* was not the cause of the involution in the improved cases.

E. W. Prosser Thomas

1112. **Study of Normal Skin with the Electron Microscope**
E. L. LADEN, I. LINDEN, and J. O. ERICKSON. *Archives of Dermatology* [*Arch. Derm.* (*Chicago*)] **71**, 219–223, Feb., 1955. 10 figs., 13 refs.

At the Veterans Administration Center, Los Angeles, ultra-thin sections of normal human skin were examined by means of the electron microscope. The appearances of the various structures are described. [For details of these and reproductions of the electron micrographs the original paper should be consulted.]

E. W. Prosser Thomas

1113. **Apparent Hepatic Dysfunction in Lupus Erythematosus**
S. KOFMAN, G. C. JOHNSON, and H. J. ZIMMERMAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 669–676, May, 1955. 4 figs., 43 refs.

1114. **Epidermolysis Bullosa Lethalis**
C. D. CALNAN. *Great Ormond Street Journal* [*Gt Ormond Str. J.*] No. 8, 113–117, 1954–5. 2 figs., 10 refs.

Paediatrics

PREMATURITY AND NEONATAL DISORDERS

1115. Controlled Clinical Trial of Effects of Alevaire Mist on Premature Infants

W. A. SILVERMAN and D. H. ANDERSEN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1093–1096, March 26, 1955. 4 figs., 6 refs.

The authors report a controlled clinical trial of a detergent mist in the treatment of premature infants over a period of 10 months at the Babies Hospital, New York. The infants, 200 in number, were assigned by means of random numbers to either a treated or a control group, those in the treated group being placed in incubators into which a solution of the detergent " triton WR-1339 " (" alevaire ") was introduced in the form of a mist, with oxygen, through a nebulizer for the infant's first 72 hours of life, while the controls were treated by the standard methods of care of the premature. In the incubators of both groups the relative humidity was 90 to 100% and the oxygen concentration from 34 to 48%. Care was taken to make the two groups similar in regard to birth weight of the infants and in other respects.

It was found impracticable to base evaluation of the trial on the clinical course of the infants and the criterion of comparison adopted was therefore the number of deaths in 72 hours. Statistical analysis of the results showed there were no significant differences between the two groups as regards the frequency distribution of ages (in hours) at death and the crude death rate; also necropsy findings, atelectasis rate, and the incidence of intracranial haemorrhage, major infections, and major anomalies were about the same in the two groups. Among the 19 infants in the treated group who came to necropsy, 9 had hyaline membrane, while this lesion was found at 6 out of 20 necropsies in the control group.

[Although this carefully controlled trial is welcome, it seems unfortunate that a method could not have been devised to keep from the observers the knowledge of which infants belonged to which group; the use of mists for both groups with numbered solutions might have solved this problem.] *David Morris*

1116. Response of Small Premature Infants to Restriction of Supplementary Oxygen

M. A. ENGLE and S. Z. LEVINE. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **89**, 316–324, March, 1955. 1 fig., 16 refs.

The need for oxygen therapy for premature infants of low birth weight was studied at the New York Hospital–Cornell Medical Center. By a modified random sampling technique 99 premature infants were assigned to one of two groups, Group 1 being kept in oxygen until they had reached or regained a weight of 1,600 g. (prolonged oxygen therapy), and Group 2 being taken out of oxygen after 5, 10, or 17 days, depending on the birth weight (curtailed oxygen therapy). For both groups withdrawal from oxygen took place gradually over a 4-day period. The average duration of oxygen therapy of infants in Group 1 was four times that of those in Group 2; the oxygen concentration for both groups did not exceed 50%. Of the infants assigned to Group 2, 7 were not withdrawn from oxygen at the appointed time, 5 because they weighed less than 1,000 g. and 2 because their condition was poor.

Subsequent progress of 75 of the infants was followed for 6 months or more and of 50 for one year or more. The gains in weight and height and the rate of motor development were similar in both groups, and there were no detectable ill-effects from early termination of oxygen therapy. The authors believe these results to indicate that routine administration of oxygen to premature infants of low birth weight is not necessary.

M. E. MacGregor

1117. The Role of Colostrum in the Nutrition of the Premature Infant. (Le rôle du colostrum dans l'alimentation du prématuré)

R. M. DU PAN, J. J. SCHEIDEGGER, E. PONGRATZ, and H. ROULET. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **12**, 243–250, 1955. 6 figs., 21 refs.

At the Institute of Hygiene, Geneva, the authors investigated the pattern of serum proteins, by means of immuno-electrophoretic analysis and paper chromatography, in 21 premature infants. They found that while there was no change in the serum levels of albumin and of α_1 and γ globulin in the first few days of life, there was a marked rise in those of α_2 and β globulin in infants fed on colostrum, only a slight increase in those fed on human milk, and none at all in those fed on cow's milk. They further showed that premature infants given colostral milk had a higher content of protein in the blood serum than in the cerebrospinal fluid. By electrophoresis colostrum was shown to contain α_2 and β globulin and a trace of γ globulin, but no albumin or α_1 globulin.

The authors conclude that the human breast is unable to produce casein during the first days of lactation and therefore draws on the maternal blood serum for the proteins essential to the suckling child, particularly α_2 and β globulins. These are produced solely in the colostrum and pass rapidly and unchanged through the neonatal intestinal walls into the blood stream. It is suggested, therefore, that colostral milk, which is easily procurable in maternity hospitals, is on account of its high protein content a useful food for premature infants, since they are less well equipped to deal with protein than full-term infants and sometimes do not tolerate the addition of amino-acids to human milk.

E. S. Wyder

1118. **An Epidemiological Study on *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*) in Premature Infants in the Presence and Absence of Infection**

E. NETER and D. H. WEINTRAUB. *Journal of Pediatrics* [*J. Pediat.*] **46**, 280–287, March, 1955. 27 refs.

Following the isolation of *Pseudomonas aeruginosa* on routine culture of swabs from premature infants in 1951, a further investigation was carried out on 143 premature infants at the Children's Hospital, Buffalo, New York. The skin, nasopharynx, throat, and rectum were swabbed twice weekly and cultures grown on agar and infusion broth. The organism was isolated from the skin of 25% of the patients, from the faeces of 51%, from the nasopharynx of 27%, and from the throat of 40%. Other studies carried out by taking swabs at different times after admission to the nursery showed that although infants rarely harboured the organism on admission, they very soon acquired it and in many cases carried it for as long as 2 weeks.

No disease was present in the majority of the infants in whom the organism was found. In 5, however, systemic disease due to it occurred and proved fatal in 4; brief reports of these cases are given. Of particular interest is the fact that 3 of the 5 infants with systemic infection had received ACTH for the treatment of retrolental fibroplasia. In the discussion attention is drawn to the potentially serious danger from *Ps. aeruginosa* once it appears in a nursery, and to the necessity of taking swabs from the nose and throat of all infants who have diarrhoea, as the causative organism is often found in those sites. *David Morris*

1119. **Pathogenic Staphylococci in the Environment of the Newborn Infant**

P. N. EDMUNDS, T. F. ELIAS-JONES, J. O. FORFAR, and C. L. BALF. *British Medical Journal* [*Brit. med. J.*] 1, 990–994, April 23, 1955. 15 refs.

The incidence and spread of staphylococcal infection among over 700 babies born in three Edinburgh hospitals and 44 born at home was studied during the period March to July, 1952. Nasal and vaginal swabs were obtained from all mothers on admission to the investigation and also on the 8th day; conjunctival swabs were taken from the babies on the 4th day after birth and umbilical swabs on the 8th day; nasal swabs were obtained from all members of medical, nursing, and domiciliary staffs. The staphylococci isolated were tested for sensitivity to sulphathiazole, chlortetracycline (aureomycin), chloramphenicol, penicillin, and streptomycin, and by study of the pattern of antibiotic resistance it was possible to trace the spread of infection.

It was found that the staphylococcal carriage rate for vaginal swabs from mothers in all three hospitals rose from 3·5% on the day of admission to 10·8% on the 8th day, but the rate for maternal nasal swabs remained the same throughout the period of study. From the conjunctival and umbilical swabs from the infants it was shown that the staphylococcal carriage rate for babies born at home was significantly lower than for those born in hospital (8·6% and 40% respectively). On the other hand nasal swabs from medical and nursing staff showed a staphylococcal carriage rate of 51% in hospital and 55% in domiciliary practice. The resistance of the organisms isolated from mothers to penicillin and other antibiotics was significantly less than that of the staphylococci isolated from babies and nursing staff.

Further analysis of the data suggested that the mother played only a small part in the spread of infection, but that there was a free interchange of staphylococci between the nursing staff and the babies, and between one baby and another. Although there were variations among the different maternity units with regard to the most frequent site of infection, infections of the eye being more common in one unit, the resistance pattern of the organisms was similar in the three units. Staphylococci isolated from two sites on the same baby were identical in only about 50% of cases, and the authors emphasize that it therefore cannot be assumed that pyogenic staphylococci isolated from one part, for example, the skin, are of the same type as those causing infection elsewhere in the body. *R. M. Todd*

1120. **Neonatal Torticollis**

W. B. KIESEWETTER, P. K. NELSON, V. S. PALLADINO, and C. E. KOOP. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1281–1285, April 9, 1955. 10 refs.

The authors are of the opinion that both the fibrous tumours of the sternocleidomastoid muscle seen in newborn infants and the muscular torticollis of older children are mainly due to abnormal presentation either during pregnancy or during labour. They suggest that the cause of fibromatosis of the sternocleidomastoid is due to ischaemia, resulting either from pressure over an area of the muscle or from an abnormal position of the foetal head in relation to the foetal body, rather than to acute trauma or haematoma. These conclusions are based on their findings in 32 infants and 14 older children at the Children's Hospital of Philadelphia. They recommend early surgical resection, the risks of which are minimal and the results good. *Franz Heimann*

CLINICAL PAEDIATRICS

1121. **Extrapyramidal Cerebral Palsy with Hearing Loss following Erythroblastosis**

R. K. BYERS, R. S. PAINE, and B. CROTHERS. *Pediatrics* [*Pediatrics*] **15**, 248–254, March, 1955. 2 figs., 13 refs.

The authors estimate that kernicterus probably accounts for about 5% of all cases of cerebral palsy and for perhaps 20% of those cases with mainly extrapyramidal involvement. Most infants with clinically recognizable kernicterus die before the sixth day of life, and in many of those who survive the physical signs may be quite mild in the neonatal period. Thus of 23 cases of cerebral palsy attributed to neonatal erythroblastosis out of a total of about 400 cases studied by the authors at the Children's Medical Center, Boston, and in private practice, only in 2 had kernicterus been diagnosed in early infancy. They maintain, however, that cases attributable to kernicterus present a characteristic clinical

picture, although this changes strikingly with age. In the neonatal period it is accompanied by hypertonus, opisthotonus, a poor Moro reflex, a high-pitched cry, and poor feeding; from 6 months to about 2 years the child shows general motor retardation with hypotonus, but has brisk tendon reflexes and usually persistent tonic neck reflexes. Athetoid movements rarely appear before the age of 18 months and may be delayed until as late as 8 or 9 years, other later features including dysarthria, lack of emotional expression, grimacing, and difficulty in swallowing.

Of the authors' 23 patients, 4 died before the age of 6. Of the remaining 19, all could walk except for 3 who were not yet 5 years old. In 11 of the 15 survivors whose intelligence could be tested satisfactorily the I.Q. was above 70. Only one of the 19 had normal hearing, the remainder having mild or severe high-tone deafness which was often suspected by the mother long before it could be demonstrated by tests, and had sometimes been responsible for under-estimation of the mental status. Twelve patients had severe or moderately severe motor defects, while 2 had virtually no physical disability; tonic neck reflexes persisted in 10 cases. Rhesus incompatibility was detected retrospectively in 20 cases and Group-A incompatibility in 3. With regard to motor training, the authors are of the opinion that "spontaneous activity, even if it is chaotic, is better than intensive physiotherapy and rigid bracing".

J. Foley

1122. **Double Alternation Performance as a Measure of Educability in Cerebral Palsied Children**

G. R. PASCAL and M. ZAX. *American Journal of Mental Deficiency* [*Amer. J. ment. Defic.*] **59**, 658–665, April, 1955. 14 refs.

1123. **Acute Hypervitaminosis A in the Infant.** (Hypervitaminose A aiguë du nourrisson)

J. MARIE, G. SÉE, and R. SAUVANT. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 251–254, Jan. 20, 1955. 24 refs.

In 1951 the authors reported (*Arch. franç. Pédiat.*, **8**, 563) that acute hydrocephalus occurred when infants were given massive doses of vitamins A and D. In the present paper they describe experiments carried out at the Hôpital des Enfants-Malades, Paris, which showed that this effect is produced by vitamin A alone. When a single oral dose of 350,000 units of natural vitamin A was given to 8 infants aged between 24 days and 18 months the following effects were observed. Within 12 to 24 hours after ingestion of the vitamin the infants showed restlessness, vomiting, and a rise in temperature, and at the same time there was bulging of the anterior fontanelle and a moderate rise in pressure in the lumbar cerebrospinal fluid (C.S.F.). Blood analysis showed a rise in serum vitamin A level up to five times the normal figure, the peak being reached 6 hours after ingestion. After 12 hours the serum level of the vitamin had fallen to about half the peak figure; vitamin A was not detected in the C.S.F. There was no correlation between blood levels of the vitamin and the severity of symptoms and signs. In 6 older infants, all under 2 years of age, in whom the fontanelle was closed much the same effects were produced.

The ingestion of a synthetic preparation of vitamin A in place of the natural vitamin evoked less striking effects and caused less increase in C.S.F. pressure. When vitamin A in the same dose was given to the infants by intramuscular injection the clinical disturbance was minimal. It appeared evident that rapid absorption of the vitamin is required to cause symptoms, and it is known that such absorption occurs readily from the alimentary tract. Determination of blood vitamin levels confirmed this point. In further experimental studies the authors obtained similar effects with the vitamin in young dogs, notwithstanding the reported observation by other workers that hypovitaminosis A causes acute hydrocephalus in the calf and the suckling pig.

In conclusion the authors point out that doses up to 70,000 units of vitamin A are always perfectly tolerated by infants. In the cases described the symptoms of overdosage were invariably transitory and innocuous, and advantage of this action of the vitamin has been taken in treating certain clinical states of cerebral hypotension, since high doses of vitamin A appear to provoke hypersecretion in the choroid plexuses.

M. E. MacGregor

1124. **The Influence of Antibiotics Given by Mouth on the Nitrogen Balance of the Infant.** (Influence des antibiotiques donnés par voie entérale sur le bilan azoté du nourrisson)

P. BERTOYE, R. FERRANDO, and H. MARBOUX. *Pédiatrie* [*Pédiatrie*] **10**, 5–9, 1955. 8 refs.

Among 113 undernourished infants treated with aureomycin for pyodermia, it was noted that 42 began to increase in weight, and that in many cases the increase was greater than would have been expected to result from control of infection alone. This observation and those of other workers on the effect of antibiotics on the nutrition of infants and young animals led the authors to investigate the influence of antibiotics on the nitrogen balance of 2 female infants.

After a preliminary period of 8 days, during which the nitrogen content of a basal diet was accurately determined, the nitrogen balance of each child was assessed on 6 successive days. Aureomycin, 0·5 g. daily, was then added to the basal diet and after an interval of 8 days the nitrogen balance was again assessed for 6 days. Finally the process was repeated with the daily addition of aureomycin, 3 mg. per kg. body weight, and procaine penicillin, 6 mg. per kg., to the basal diet. Both infants had a positive nitrogen balance when taking the basal diet without antibiotics. When aureomycin alone was added the balance in one case was unchanged, and in the other it was increased by 43%. When both penicillin and aureomycin were added the nitrogen balance of the first baby increased by 27% and that of the second by 18%.

Experiments which the authors are conducting on chicks have provided evidence suggesting that antibiotics facilitate the absorption of nitrogen from the intestine,

and at the same time permit increase in the numbers of certain bacteria in the intestinal flora which supply a hitherto unknown growth factor to the young organism. Clinical experience indicates that the antibiotics are of most value when added to the diet of infants under 6 months of age who are debilitated as a result of faulty feeding. *E. S. Wyder*

1125. **Coeliac Disease. The Relative Importance of Wheat Gluten**
C. A. C. Ross, A. C. Frazer, J. M. French, J. W. Gerrard, H. G. Sammons, and J. M. Smellie. *Lancet* [*Lancet*] **1**, 1087–1091, May 28, 1955. 1 fig., 16 refs.

Of 30 children with active coeliac disease all but 2 responded to diets free from wheat gluten. The main diagnostic criterion was chronic steatorrhoea with normal pancreatic function; and the main therapeutic criterion was disappearance of the steatorrhoea.

In the children who recovered on a wheat-gluten-free diet improvement in fat absorption coincided with improvement in chylomicrograph, standard weight for age, and haemoglobin level, and with diminution in the dilatation of the small intestine, but not with any significant improvement in the glucose-tolerance test. Of the 2 children who did not respond to the diet, 1 appeared to have a deficiency of bile salts and the other child showed fat intolerance.

The term " gluten-induced coeliac disease " is suggested for the disorder in those children who recover on diets free from wheat gluten.—[Authors' summary.]

1126. **Curable Subacute Anaemia of Infants with Medullary Hypoplasia and Hepatosplenic Haematopoiesis.** (L'anémie subaiguë curable du nourrisson avec hypoplasie médullaire et hématopoïèse hépatosplénique)
C. Sarrouy, R. Cabannes, L. Sendra, and M. Lalanne. *Pédiatrie* [*Pédiatrie*] **10**, 11–24, 1955. 1 fig., 9 refs.

The authors report in detail 6 cases, occurring in North African infants aged 6 to 18 months, of a type of medullary hypoplasia not hitherto described. Severe anaemia with intense pallor of the skin and mucous membranes was present in all 6 infants, who were grossly undernourished and rachitic. The most prominent finding was enlargement of the spleen down to the anterior superior iliac spine, and of the liver to 4 finger-breadths below the costal margin. Both organs were of firm consistency. The blood picture was that of a hypochromic microcytic anaemia with thrombocytopenia but without leucopenia, and bone-marrow biopsy revealed hypoplasia and frequently aplasia. Splenic and hepatic puncture showed these organs to be the sites of intense haematopoiesis. Radiological evidence of florid rickets was present in the epiphyses, and Looser's zones were seen in the diaphyses.

No form of treatment, except possibly blood transfusion, appeared to have any effect on the anaemia, the debility, or the rickets, all of which, however, eventually underwent spontaneous cure. The anaemia regressed after some 8 months in hospital, with restoration of bone-marrow function and diminution in size of the liver and spleen. The infants' general condition improved slowly but progressively, and all rachitic signs finally disappeared.

All these infants had been born at full term, but their mothers belonged to a poverty-stricken community and had suffered severe privation during pregnancy and the puerperium, while their notions of artificial feeding were rudimentary. It is to these factors that the authors attribute the infants' condition, which they consider to be a " physiological fixation " of the bone marrow with undue persistence of normal embryonic haematopoiesis rather than a truly pathological state, its clinical features becoming manifest only after the 6th month, which is the critical point in an infant's life when such reserves as were supplied by the mother during foetal life are exhausted and it must rely on its own metabolic processes.

The differential diagnosis between this syndrome and other infantile aplastic anaemias, bone diseases, and parasitic infections is fully discussed. *E. S. Wyder*

1127. **Changes in the Flat Bones of the Skull in Blood Disorders, Especially Anemia, of Childhood.** [In English]
M. Kunnas. *Annales paediatriae Fenniae* [*Ann. Paediat. Fenn.*] **1**, 1–87, 1955. 18 figs., bibliography.

1128. **Posterior Pituitary Snuff Treatment of Nocturnal Enuresis**
F. G. W. Marson. *British Medical Journal* [*Brit. med. J.*] **1**, 1194–1195, May 14, 1955.

At the University of Leeds 4 healthy, intelligent, and psychiatrically well-adjusted adolescents suffering from persistent and frequent nocturnal enuresis were treated with pituitary snuff (" di-sipidin ") for 6 to 9 months and the results compared with those observed during administration of a placebo snuff. During administration of pituitary snuff the incidence of nocturnal enuresis fell considerably in all 4 cases, the reduction being highly significant statistically in 3 and less so in one. No toxic effects were observed. The author believes the results to indicate that pituitary snuff will prove of great value in the treatment of certain adolescent and adult cases of nocturnal enuresis. *John Lorber*

1129. **Chlorpromazine in the Treatment of Emotionally Maladjusted Children. Preliminary Report**
R. L. Gatski. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1298–1300, April 9, 1955. 7 refs.

For the treatment of emotionally maladjusted and severely disturbed children the author recommends the oral administration of chlorpromazine in an initial dose of 10 mg. once daily, increasing during the first week to 10 or 20 mg. 4 times daily, this dosage being continued for 3 to 4 weeks. He reports the results obtained in 9 children aged from 6 to 13 years. After one week's treatment their behaviour improved and they became calmer and more cooperative. No side-effects and no complications were observed. From this preliminary trial it is concluded that chlorpromazine " has a definite place in the treatment of emotionally maladjusted children ". *Franz Heimann*

Medical Genetics

1130. The Genetic Basis of Various Types of Ichthyosis in a Family Group

H. O. CURTH and M. T. MACKLIN. *American Journal of Human Genetics* [*Amer. J. hum. Genet.*] 6, 371–382, Dec., 1954. 5 figs., 24 refs.

The index cases in the study reported here from Columbia University, New York, and Ohio State University, Columbus, were 2 brothers who were born with ichthyosis hystrix and showed in addition certain features of congenital ichthyosiform erythroderma and, in the elder brother, of epidermodysplasia verruciformis. The diagnosis was made by physical examination and by skin biopsy. After examination of other members of the family a pedigree diagram, extending over 5 generations, was constructed. Mild or severe cutaneous anomalies, occurring either as localized hyperkeratoses or as generalized ichthyosis (hystrix or simplex), were present in one sister, the mother, 2 of the mother's 7 brothers and one of her 2 sisters, and also in male and female offspring of the mother's affected sister. The condition was fully manifest only in males, and in general the males of this family were more severely affected than the females. The pedigree shows that none of the offspring of normal parents were affected. The incidence of other congenital malformations and of allergic conditions in the family was high.

The authors postulate a single main gene as responsible for the condition occurring in this family, and point out that the distribution is consistent with transmission by an autosomal dominant with expressivity variable in both sexes, but more complete in the male.

R. H. Cawley

1131. The Familial Occurrence of Hypertension and Coronary Artery Disease, with Observations Concerning Obesity and Diabetes

C. B. THOMAS and B. H. COHEN. *Annals of Internal Medicine* [*Ann. intern. Med.*] 42, 90–127, Jan., 1955. 8 figs., bibliography.

An unselected group of 266 clinical students at the Johns Hopkins Medical School, Baltimore, supplied information (obtained in consultation with their families) on the occurrence of hypertension, coronary arterial disease, obesity, and diabetes among their parents, grandparents, and parental sibs, each disease being marked as "definitely present", "probably present", "definitely not present", or "unknown" for each individual. The incidence of these 4 conditions in a population consisting of 532 parents, 1,064 grandparents, and 1,595 parental sibs was then tabulated and analysed in some detail statistically and genetically. The authors were thus able to estimate directly the incidence of single disorders in the parents' and grandparents' generations, the age-differences between affected and non-affected groups in each generation, the incidence of combined disorders occurring in the same individual, and for each disorder the incidence among sibs of affected and of unaffected parents and among the offspring of the four types of grandparental mating.

The incidence (expressed as percentage) of the various diseases among parents (mean age 55 years) and grandparents (mean age 70 years) respectively were as follows: hypertension, 12·0 and 20·6 (slightly higher in females than in males); coronary arterial disease, 5·5 and 16·9 (significantly higher in males); hypertension and/or coronary arterial disease, 16·0 and 30·7; obesity, 12·2 and 9·3 (slightly higher in males of parents' and females of grandparents' generations); diabetes, 2·4 and 4·1 (sex differences as for obesity).

Each of the disorders studied occurred significantly more frequently among the offspring of parents affected with that disorder than among the offspring of parents not so affected, the incidence being highest when both parents were affected. These rates were standardized for age of parents. The authors were able to demonstrate an association between hypertension and obesity, in both individuals and families, and a less significant correlation between hypertension and coronary disease.

With regard to the genetical analysis, the result of the application of Snyder's formulae to the data was inconclusive: the presence of a single autosomal gene governing any of the disorders could neither be proved nor disproved. The authors suggest that the data indicate a more complex aetiology involving interactions in which variables in both genotype and environment are of importance.

R. H. Cawley

1132. A Genetic Study of Progressive Spinal Muscular Atrophy

N. C. MYRIANTHOPOULOS and I. A. BROWN. *American Journal of Human Genetics* [*Amer. J. hum. Genet.*] 6, 387–411, Dec., 1954. 12 figs., 34 refs.

The authors discuss the clinical classification of types of progressive muscular atrophy, and review at some length the reports of familial incidence appearing in the literature and the suggested genetic mechanisms. Two pedigrees are presented and discussed in detail, the propositi having been patients at the University of Minnesota Hospitals. In these families the condition was common, and in about half the affected members 2 or all of the possible manifestations (spinal form, progressive bulbar paralysis, and progressive external ophthalmoplegia) occurred. The age of onset of the condition was very late (50 to 60 years) in these particular families, so that the pedigrees are incomplete in that the incidence in the fourth and fifth generations will not be known for a number of years. In other respects, the pedigrees are consistent with the supposition that all the types of progressive muscular atrophy here encountered were manifestations of the action of a single autosomal dominant gene, probably with full penetrance, and with higher expressivity in the male.

R. H. Cawley

Public Health

1133. **Mortality and Marital Status**
D. SHURTLEFF. *Public Health Reports* [*Publ. Hlth Rep. (Wash.)*] **70**, 248–252, March, 1955. 1 fig., 2 refs.

The author has estimated the average annual number of deaths of single, married, widowed, and separated or divorced persons over 20 years of age in the United States in the years 1949–51 and related these figures to the distribution of the total population by marital status shown by the 1950 census. Sex and age differentials are shown for each marital class.

At all ages and for both sexes the death rate was lowest among married persons, followed by single persons; it was highest among widowed persons under 60 years of age and divorced persons over that age. For the population as a whole, standardized by age, taking the expected number of deaths among the married group as 100, the rates for males and females respectively were: single, 163 and 124; widowed, 185 and 155; and divorced, 207 and 155.

Age-specific mortality figures for single, married, widowed, and divorced persons of each sex are tabulated and show the magnitude and direction of differentials according to age, sex, and marital status. Comparison with figures for 1940 shows the expected secular decline occurring in all groups except unmarried males over 45 years of age. There is some difference between the patterns of mortality as associated with marital status in 1940 and in 1950, due presumably to changes in factors affecting both mortality and marital status itself.

R. H. Cawley

1134. **Comparative Fatality of Poliomyelitis in Families with Single and Multiple Cases**
M. SIEGEL and M. GREENBERG. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1080–1083, March 26, 1955. 1 fig., 18 refs.

Case mortality from poliomyelitis in New York City among families with only one case of the disease was compared with that among families having more than one case. The figures analysed covered the 5-year period 1949–53, when 5,563 cases of poliomyelitis were reported with 321 deaths, an over-all mortality of 5·8%; 1949 was an epidemic year with 2,446 cases and 179 deaths. The authors state that over the 5-year period mortality from all forms of the disease, including non-paralytic forms, increased with age.

Of the 5,563 cases, 5,181 were single cases in a family and 382 were multiple; the mortality in these two groups was 5·6% and 8·1% respectively, the difference being statistically significant. When the relationship between age and increased mortality in multiple cases was studied it was found that for all ages combined there was a 50% increase in the observed number of deaths over the number expected, the increase being most marked in patients over 15 years of age. It was also found that the incidence of, and mortality from, bulbar poliomyelitis were significantly higher in multiple cases than in single cases and in patients over 15 years than those under this age.

The authors consider that " some host or environmental factor associated with age was responsible for the results " and that they were related in part to " the order in which the multiple cases occurred in the household ".

F. T. H. Wood

1135. **Pharyngoconjunctival Fever. Epidemiological Studies of a Recently Recognized Disease Entity**
J. A. BELL, W. P. ROWE, J. I. ENGLER, R. H. PARROTT, and R. J. HUEBNER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1083–1092, March 26, 1955.

From the National Microbiological Institute, Bethesda, Maryland, a study is reported of over 300 cases of an acute, communicable, respiratory illness characterized by fever lasting 4 to 6 days, by pharyngitis, and by conjunctivitis lasting one to 3 weeks, these symptoms occurring singly or in combination. Adenoidal-pharyngeal-conjunctival (A.P.C.) Type-3 virus was recovered from swabs from the eye, throat, and anus in 80 cases, and a specific serological antibody response was obtained in practically all patients tested. The cases occurred in the summer of 1954 in a children's day camp and two residential neighbourhoods in and around Washington, D.C. There were localized epidemics and sporadic cases, and the condition was observed in all age groups (but predominantly in children) and in both sexes. The incubation period appeared to be 5 or 6 days and the period of communicability to be limited to 10 days. Details are given of the results of bacteriological studies, and a table shows that of the 80 cases from which the virus was recovered, fever was present in 72, conjunctivitis in 53, and sore throat in 56. There were no deaths and no sequelae were recognized.

Summarizing their findings the authors state that A.P.C. Type-3 virus was associated with the particular clinical syndrome described and not with other common illnesses; it was not present in healthy persons and was found almost exclusively during the acute stage of the illness. They suggest that this disease entity should be termed " pharyngo-conjunctival fever ".

F. T. H. Wood

1136. **The Epidemic of Poliomyelitis in Greenland 1953**
B. ESKESEN and B. GLAHN. *Danish Medical Bulletin* [*Dan. med. Bull.*] **2**, 46–51, March, 1955. 2 figs., 4 refs.

1137. **The Transmission of Hepatitis Virus by Routine Immunization Procedures**
F. P. ELLIS. *Journal of Hygiene* [*J. Hyg. (Lond.)*] **53**, 124–128, March, 1955. 9 refs.

Industrial Medicine

OCCUPATIONAL DISEASES

1138. **Anthracosilicosis, with Special Reference to Pulmonary Cavitation**
N. M. WALL. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 544–555, April, 1955. 12 refs.

This paper [written without reference to recent literature on the subject] describes 15 cases of pulmonary cavitation in anthracosilicosis and confirms the generally accepted view that such cavitation is not usually tuberculous. The author also suggests that since 4 cases of bronchogenic carcinoma occurred in 100 consecutive necropsies on anthracosilicotic patients, whereas the incidence of bronchogenic carcinoma in the general male population of the hospital during the same period was only 0·23%, anthracosilicosis may predispose to this form of cancer. [This conclusion is invalid since it is based upon a comparison of figures derived from dissimilar populations.] *C. M. Fletcher*

1139. **The Prophylaxis of Progressive Silicosis.** (О профилактике прогрессирования силикоза)
V. V. GERBST, A. A. LOPATINA, K. S. ISMAGULOVA, and L. V. BRATUKHINA. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 29–32, April, 1955. 11 refs.

The most serious industrial disease among miners is silicosis, and in the U.S.S.R. the problem is being dealt with by treatment in special sanatoria where the patients are given three courses of combined therapy extending over 2 years. This treatment consists in graduated exercise in a sunny and bracing climate combined with physiotherapy, ultraviolet irradiation, an adequate diet, and the administration of nicotinic acid—on which great stress is placed, Genkin having recommended the use of nicotinic acid and ascorbic acid in silicosis, since they are thought to act upon the oxidation processes of the whole body and to stimulate blood formation. The present authors also emphasize the vasodilator properties of these vitamins, nicotinic acid being said to dilate especially the blood vessels of the lungs and to improve the pulmonary circulation [but whether this is exercised through the bronchial or the pulmonary vessels is not stated].

In the study here reported from the Gornyak Silicosis Sanatorium 27 patients were observed, 14 of whom were in the first stage and 13 in the second stage of the disease; 17 of them had already been transferred to non-dusty work before admission to the sanatorium, while the remaining 10, after one or more courses of treatment, had been able to continue for some time at their usual employment. As a result of the treatment described above the vital capacity of these patients increased at the end of 2 years by an average of 620 ml. above that on admission, while the breath-holding time increased by 10 seconds, the chest expansion from 3·2 to 6·4 cm., and the body weight by 4 to 6 kg. The erythrocyte sedimentation rate (E.S.R.) was found to be increased not only in cases of silico-tuberculosis, but often also in the absence of tuberculosis. A rise in the E.S.R. following treatment may occur, however, and is then suggestive of tuberculosis. Capillaroscopic studies showed an increase in the number of capillaries per field, although normally in this disease the number tends to fall with the progress of the fibrosis. At the end of the third course the exercise tolerance test was normal in regard to both pulse and respiration rates. Radiological examination at the end of the 2-year period showed that the progress of the disease had been halted, and in some cases the radiological appearances were much improved.

The authors claim that this combined system of treatment by climatic, physiotherapeutic, dietetic, and above all psychological means has fully justified itself. Its curative value depends not only on adequate ventilation of the lungs with fresh air and removal from harmful surroundings, but on the building up of the patient's morale and his confidence in the efficacy of the treatment.

[Although the value of nicotinic acid is so strongly emphasized the dosage employed is not mentioned.]
L. Firman-Edwards

1140. **The Adsorption of Serum Proteins on to the Surface of Silica and its Possible Importance in the Pathogenesis of Silicosis.** (L'adsorbimento delle sieroproteine alla superficie della silice; sua possibile importanza nella genesi della silicosi)
B. PERNIS and M. BATTIGELLI. *Medicina del lavoro* [*Med. d. Lavoro*] **46**, 1–13, Jan., 1955. 3 figs., 29 refs.

In view of recent hypotheses regarding the pathogenesis of silicosis which are based on the adsorption of proteins by silica, the authors, in a study carried out at the University of Milan, attempted to ascertain which of the proteins normally present in organic fluids are most readily adsorbed on to the surface of silica. By means of ultraviolet photometry with a Beckmann spectrophotometer, the quantity of serum albumin and gamma globulin adsorbed by a given quantity of quartz powder and by finely divided amorphous silica was determined, a 0·1% solution of albumin or gamma globulin in 0·9% saline at *p*H 7 being used for the adsorption experiments. It was found that the quantity of gamma globulin adsorbed was 2 to 3 times that of serum albumin adsorbed under the same conditions, and also that with surfaces of equal area quartz adsorbed a much larger amount of protein than did amorphous silica.

Adsorption experiments were therefore undertaken in which whole human serum was percolated through columns of carbon, quartz, and amorphous silica. By electrophoretic analysis it was shown that the protein composition of the fluid flowing from the carbon column

was similar to that of untreated serum, but that the fluid from the quartz and silica columns showed elective adsorption of serum globulins, and particularly of gamma globulin. It is considered probable that adsorption on quartz or silica is followed by denaturation of the adsorbed proteins and that this phenomenon may be important in the pathogenesis of silicosis.

L. G. Norman

1141. **Pneumoconiosis Caused by Inhalation of Apatite Dust.** О развитии пневмокониоза от вдыхания апатитовой пыли (Клинические и экспериментальные наблюдения)

A. V. GRINBERG. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] 75–80, No. 2, March–April, 1955. 5 figs.

The observed fact that the inhalation by miners of apatite dust gives rise to a nodular pneumoconiosis and the further fact that pneumoconiosis develops in laboratory animals following the inhalation of apatite dust appear to the author to invalidate the theory of the specificity of quartz as the only cause of fibrosis of the lungs in cases of pneumoconiosis. He states that the radiographic picture of apatite pneumoconiosis differs essentially from that observed in pneumoconiosis due to other causes. Early radiological recognition of the condition is favoured by the rapid development of the nodules and their relatively high opacity to *x* rays.

A. Orley

1142. **Management and Treatment of Patients with Coal-workers' Pneumoconiosis**

J. C. GILSON and G. S. KILPATRICK. *British Medical Journal* [*Brit. med. J.*] **1**, 994–999, April 23, 1955. 11 refs.

In 1947 there were 16,000 certified cases of coal-workers' pneumoconiosis in South Wales. The number of new cases certified each year had risen steadily from 44 in 1931 to 5,224 in 1945, but declined to 1,079 in 1953, in which year there were 2,987 cases in the rest of Great Britain. In view of this increasing incidence, the authors, members of the Medical Research Council Pneumoconiosis Research Unit, Llandough Hospital, Glamorganshire, offer this paper as a guide to medical practitioners unacquainted with the condition who may be asked for advice by patients who are or have been coal-miners.

They classify the disease into two varieties: (1) simple pneumoconiosis, with collections of dust and focal emphysema most marked in the upper and mid-zones; and (2) complicated pneumoconiosis, in which there is massive fibrosis, suspected to be of tuberculous origin. In South Wales 1 to 2% of men with simple pneumoconiosis develop complicated pneumoconiosis every year. Tubercle bacilli may be isolated from 40% of cases at necropsy, but from less than 10% coming to hospital. Thus prevention of serious disability depends on reducing exposure to coal dust and eliminating the risk of infection by tuberculosis.

Increasing breathlessness on exertion, cough, pain in the chest, and lassitude in a man who has worked in the mines should raise the suspicion of pneumoconiosis. Under the National Insurance Industrial Injuries Act (1946) a miner suffering from this disease receives disablement benefit for life, his disability being expressed on a percentage basis starting at 1% and graded in steps of 10% to 100%. This is unaffected by his subsequent earnings and he may, if he wishes, continue to work underground under "approved" conditions. Supplementary benefits are also payable in special cases. [For full details of compensation provisions and advice on employment of disabled miners the original should be consulted.]

Treatment should primarily be directed to controlling bronchospasm and respiratory infection. For the former adrenaline, atropine, and aminophylline have been found most useful. Acute pulmonary infection can be best controlled by penicillin in large doses—2 mega units of combined procaine and crystalline penicillin daily—with streptomycin, 1 to 2 g. daily. Cough, especially troublesome in the early morning, may be relieved by adding a simple sodium chloride compound mixture to a cup of tea or glass of hot water.

Pain in the chest is a common symptom, and may be due to pleurisy, local injury, cardiac ischaemia, or pulmonary hypertension. During convalescence from an episode of chest infection breathing and general exercises are of value in restoring confidence. When the disease is complicated by tuberculosis antituberculous chemotherapy is indicated, though the outlook is poor in these cases. Cor pulmonale is often the terminal stage of complicated pneumoconiosis, and is best treated by rest in bed with a salt-poor diet and the administration of digitalis and mercurial diuretics. Oxygen therapy is of considerable help in this condition and can usually be given without risk.

Kenneth M. A. Perry

1143. **Pathological Studies of Modified Pneumoconiosis in Coal-miners with Rheumatoid Arthritis (Caplan's Syndrome)**

J. GOUGH, D. RIVERS, and R. M. E. SEAL. *Thorax* [*Thorax*] **10**, 9–18, March, 1955. 10 figs., 12 refs.

After summarizing, for comparative purposes, the pathological features of coal-workers' pneumoconiosis with and without associated tuberculosis the authors, writing from the Welsh National School of Medicine, Cardiff, describe the morbid anatomy of the lungs of 16 such workers who also had rheumatoid arthritis. Tuberculosis was certainly present in 3 cases and probably in 2 others. Corresponding with the opacities originally described by Caplan in the radiograph of the chest in such cases were distinctive gross lesions which were fairly characteristic of pneumoconiotic nodules and showed no specifically "rheumatoid" features. They differed, however, both macroscopically and microscopically, from the "infective nodules" (orthodox collagenous nodules) of the ordinary coal-workers' pneumoconiosis complicated by tuberculosis in containing necrotic collagen and dust, with non-specific inflammation. These differences are thought to be due to the abnormal reaction of the rheumatoid arthritic to the collagen produced in infective pneumoconiosis.

A. C. Lendrum

1144. **The Effectiveness of Dust Control in Wet Boring in the Coal Mines of the Don Basin.** (Об эффективности обеспыливания при бурении с промывкой на угольных шахтах Донбасса)
K. A. GALKINA. *Гигиена и Санитария* [*Gigiena*] 20–23, No. 4, April, 1955. 1 fig.

Wet boring is now widely employed in the coal mines of the Don basin, and has largely replaced boring with forced air down-draught. A substance called " OP7 ", a paste-like material which dissolves in water without residual sediment, is employed for irrigation during the boring and is more effective when sprayed on the sides of the shaft than when directed axially. It lowers the surface tension of all kinds of water—distilled water, tap-water, and mine water were tested—and the optimum concentration is 0·05%, stronger solutions being less effective in laying the dust than water alone. The best rate of spraying is 0·3 to 0·5 litres per minute, this resulting in the dust content of the air being reduced to 55·5% of that obtained with simple water spraying, which itself was reduced to 83·8% of that caused by dry boring with forced air down-draught. The experiments were carried out in a boring through coarse grits with a high (65%) silica content.

[The composition of " OP7 " is not revealed.]

L. Firman-Edwards

1145. **Fluorine Compounds in the Air of Electrolysing Rooms of Aluminium Factories.** (Фтористые соединения в воздухе электролизных цехов алюминиевых заводов)
A. P. BESSONOVA. *Гигиена и Санитария* [*Gigiena*] 23–28, No. 4, April, 1955. 1 fig., 8 refs.

While adequate extraction-ventilation apparatus near the electrolysing baths in aluminium works can prevent the accumulation of fumes containing fluorine compounds for most of the time, this is not so during the process of " cultivation " of the bath, when the crust of electrolyte is broken and fresh ore is added. This work is performed by hand, and the cultivation of each bath takes a team of 2 or 3 workers about one hour; a single team may thus work on three, four, or more baths in a day. In the study here reported estimation of the concentration of fluorine compounds in the air of workshops where the electrolysing baths were situated gave average values of 0·0066 mg. per litre in winter and 0·0015 mg. per litre in summer, the difference being due partly to better general ventilation during the warmer summer months and partly to more efficient working of the extraction fans in summer (10,000 c. metre per hour as against 6,000 in winter). The introduction of a system of forced intake ventilation in the workshops reduced the fluorine concentration to 0·0025 mg. per litre in winter and to 0·0007 mg. per litre in summer.

The amount of fluorine inhaled by workers was then estimated by determining the concentration of fluorine in the urine and measuring the total daily urinary output in 24 hours. This showed that whereas in control workers having no direct contact with fluorine fumes the urinary concentration of fluorine was 0·88 mg. per litre and the mean 24-hour output 1·26 mg., and in newly arrived workers with less than 10 days' exposure to fumes the average 24-hour output was 3·62 mg., the 24-hour excretion of fluorine by workers who had been some months in the workshops amounted to 5·38 mg. in summer and 5·60 mg. in winter. Moreover, these high figures continued for some time after the subjects had been removed from exposure, so that some degree of storage of fluorine must occur.

In discussing the prevention of fluorine poisoning in workers in electrolysing plants the author points out that this can be achieved by taking technological measures to increase mechanization of the method of replenishment of the baths, and by shortening the hours of exposure. Besides this, there should be improved construction of ventilating fans, and a better combination of extraction and forced ventilation, particularly during the winter months. *L. Firman-Edwards*

1146. **Hazards and Occupational Diseases in the Production and Handling of Certain Plastic Materials.** (Rischi e patologia professionale nella produzione e nella lavorazione di alcune materie plastiche)
L. PARMEGGIANI and C. SASSI. *Medicina del lavoro* [*Med. d. Lavoro*] **46**, 14–24, Jan., 1955. 1 fig., 12 refs.

Writing from the Department of Industrial Hygiene, University of Milan, the authors review the main occupational hazards which may arise during production and handling of the plastics polyvinyl chloride, polystyrene, "nylon", and cellulose acetate.

In the production of polyvinyl chloride only slight signs of nasopharyngeal irritation were observed in workers who were employed in filling sacks with the finished powder. In spinning operations the employees were exposed to concentrations of acetone ranging from 15 to 90 p.p.m. and to concentrations of carbon disulphide of from 25 to 200 p.p.m. Irritability, tremors, and exaggerated reflexes, together with congestion of the conjunctival and nasopharyngeal mucosae and some generalized bronchitis were found in employees with an average exposure of one year's duration.

In the production of polystyrene, workers exposed to concentrations of ethylbenzene of from 70 to 275 p.p.m. showed similar signs of irritability of the central nervous system, some degree of leucopenia with a relative lymphocytosis, and, rarely, dermatitis. Employees exposed to styrene in concentrations somewhat lower than 200 p.p.m. suffered from dermatitis and signs of mucosal irritation, but the blood picture was normal. The aluminium chloride used in the process of ethylation of benzene caused bronchospasm and delayed healing of wounds. The authors recommend a maximum allowable concentration, for prolonged exposure, of 100 p.p.m. for ethylbenzene and 150 p.p.m. for styrene.

Concentrations varying from 0·1 to 1·9 p.p.m. of diphenyl and diphenyl oxide vapours were found in the atmosphere of workrooms during the polymerization and spinning of nylon. Such concentrations resulted in conjunctival and nasopharyngeal irritation in exposed workers, but are not considered liable to cause systemic intoxication. Some of the finishing departments were very noisy (up to 105 decibels).

In the production of cellulose acetate hazards arise in the acetylation of the cellulose and the filtering of the colloidal product. In the former process the operation is carried out in an atmospheric concentration of 75 to 260 p.p.m. of acetic acid and many workers suffered from severe mucosal congestion, catarrhal bronchitis (sometimes with bronchospasm), gastric disturbances, pigmentation of the skin of the palms, and dental erosion. During the filtration of the colloid the concentration of acetone reached 920 p.p.m. and the exposed employees showed signs of mild nervous and gastric disturbances, mucosal irritation, and bronchitis. In the case of 2 employees examined for urinary and respiratory excretion of acetone it was found that elimination was not completed during the rest between one working shift and the next, but only during the longer weekend rests. The authors accordingly suggest that the maximum allowable concentration of acetone of 500 p.p.m. recommended by American authorities should be enforced.

L. G. Norman

See also Pathology, Abstract 922.

INDUSTRIAL TOXICOLOGY

1147. **Toxicological Studies of Certain Substitutes for Benzene as a Solvent. II. Toluene.** (Recherches toxicologiques sur les solvants de remplacement du benzène. II. Etude du toluène)

R. Fabre, R. Truhaut, S. Laham, and M. Péron. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mal. prof.*] **16**, 197–215, 1955. 6 figs., bibliography.

In order to determine the relative hazards involved in the industrial use of toluene as a substitute for benzene (benzol), a study was made at the Laboratory of Toxicology and Industrial Hygiene, Paris, of chronic toluene intoxication by inhalation in three species of experimental animals which were exposed to various concentrations of the vapour for 8 hours a day, 6 days a week, for periods up to 6 months. The vapour was of pure toluene, although the substance used in industry usually contains a variable proportion of benzene.

In rats and rabbits exposed to toluene in concentrations of 1·5 to 8 mg. per litre of air for 7 weeks no significant changes were found in the blood cells or in the bone marrow. The blood coagulation time was slighly prolonged, although the calcium level, thrombin value, and platelet count were normal. At necropsy the only pathological finding was a moderate oedema of the lungs.

Two dogs similarly exposed to toluene vapour in a concentration of 7·5 mg. per litre of air for 4 months showed no sign of distress other than a slight irritation of the eyes and nose. The concentration was then increased for a further 2 months to 10 mg. per litre, and this resulted in a loss of coordination and slight paralysis of the hind quarters. The 2 dogs died within 24 hours of each other at the end of the 6th month of the experiment. They had continued to gain weight throughout the experiment, no alteration was found in the blood cells or in the bone marrow, and the blood coagulation time remained within normal limits. At necropsy the heart, lungs, liver, spleen, and kidney all showed some congestion; in the kidney there was swelling of the glomeruli and some blood casts were present. (It is pointed out that the dogs used were not bred for the purpose but were strays and that such animals are often subject to interstitial nephritis.) In the spleen there was a diminution of the lymphoid follicles and some haemosiderosis.

The quantity of toluene in the organs of these dogs was determined within 12 hours of death by a method of nitration and extraction with butanone, which is described in detail. The results, expressed as mg. of toluene per gramme of tissue, were as follows: adrenal glands, 20; cerebellum, 19; bone marrow, 18; cerebrum, 18; liver, 14; blood, 9; kidney, 7; spleen, 6·8; lung, 6·6; thyroid gland, 3·5; hypophysis, 1·7.

The authors conclude that, with due regard to the fact that these results were obtained in animals and also that high concentrations of toluene clearly had some toxic effect upon the nervous system, nevertheless, on account of the complete absence of signs of damage to haematopoietic tissues, it is preferable, for reasons of safety, to use toluene in place of benzene in industry.

M. A. Dobbin Crawford

1148. **The Toxicity of Diethylamine.** (О токсичности диэтиламина)

O. G. Vasileva. *Гигиена и Санитария* [*Gigiena*] 28–31, No. 4, April, 1955.

Diethylamine, which is being used to an ever increasing extent in industry, has highly toxic properties. The author has studied the mortality of white mice exposed to varying concentrations of diethylamine vapour and to contact with the liquid. Among mice, in batches of 20, exposed to the vapour in concentrations varying from 3 mg. to 15 mg. per litre the number of deaths ranged from 2 to 20 (100%). Some of the mice subjected for 2 hours to the lower concentrations (3 to 5 mg. per litre) survived up to 14 days, but at the highest concentration (15 mg. per litre) all of them died in the first 5 days. The post-mortem changes included congestion and oedema of the lungs, congestion of the brain, liver, and spleen, and in animals surviving for a few days there was also fatty degeneration of the liver epithelium and localized necrobiosis.

In a further study, in which the change in conditioned reflexes was taken as an index of toxic disturbance from diethylamine, the author and her fellow-workers found a marked disturbance in established conditioned reflexes after exposure of the mice to a vapour concentration as low as 0·3 mg. per litre, these effects lasting up to one month after exposure. She therefore regards 0·3 mg. per litre as the threshold of toxicity, and 3 mg. per litre as the minimum lethal concentration for the vapour. The severe effects of splashes of liquid on the skin and eyes are also described. It is urged that every effort be made to minimize exposure to diethylamine vapour and that accidental contact of the liquid with the skin and eyes of workers using this toxic substance must be prevented.

L. Firman-Edwards

Forensic Medicine and Toxicology

1149. **Distribution of Lead in Blood as Affected by Edathamil Calcium-disodium**
S. P. BESSMAN and E. C. LAYNE. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **89**, 292–294, March, 1955. 1 fig., 13 refs.

In this paper from the Research Foundation of the Children's Hospital, Washington, D.C., the authors report observations of the blood level and urinary excretion of lead in 5 patients with lead poisoning who were given a single subcutaneous injection of 1 g. of the calcium disodium salt of ethylenediaminetetraacetic acid (" edathamil ") as a 1% solution in saline. Within the blood the distribution of lead was altered in such a way that the lead content of the erythrocytes fell and that of the plasma rose, the plasma level reaching a peak at the second hour. Nevertheless, the plasma clearance of lead was not strikingly increased, which suggested that the compound of lead and chelating agent formed an additional linkage to a protein component of the plasma, thereby impeding its excretion by the kidneys.
M. E. MacGregor

1150. **Acute Intestinal Iron Intoxication. I. Iron Absorption, Serum Iron and Autopsy Findings. II. Metabolic, Respiratory and Circulatory Effects of Absorbed Iron Salts**
K. R. REISSMANN, T. J. COLEMAN, B. S. BUDAI, and L. R. MORIARTY. *Blood* [*Blood*] **10**, 35–45 and 46–51, Jan., 1955. 3 figs., 36 refs.

The increasing number of children's deaths due to the ingestion of iron salts prompted this investigation, carried out at the University of Kansas, into the mechanism of acute intestinal iron intoxication. In the first paper the authors describe experiments in which ferrous sulphate and chloride were given by stomach or duodenal tube or by enema to rabbits and dogs and the absorption of these salts was studied. In both species and by both routes the lethal dose was about 200 mg. Fe per kg. body weight. Although only a small fraction of the total dose was absorbed, the serum iron level rose rapidly after administration of the ferrous salt, the rise being roughly proportional to the dose. Survival time, which varied inversely with the dose, was 9 to 18 hours after administration of 200 mg. Fe per kg. and was as short as 3 hours after 750 mg. Fe per kg. Most of the serum iron was " non-beta$_1$-globulin bound " and was in the ferric state.

The local changes seen in the gut at necropsy did not appear to be sufficient to account for death and the authors suggest that death was due to a toxic action of iron exerted after its absorption. A study of this aspect of the problem is reported by two of the authors in the second paper. It was found that the duodenal or rectal administration of toxic doses of dissociable ferrous salts produced acidosis. An increase in the respiratory rate and minute volume, with a lowering of the plasma carbon dioxide content and an excessive carbon dioxide output, was observed. The blood levels of glucose, lactate, and citrate were raised. The cardiac output fell progressively but the blood pressure was maintained until death, which was due to respiratory failure. *H. B. Stoner*

1151. **Fatal Fulminant Acute Carbon Tetrachloride Poisoning**
R. B. JENNINGS. *Archives of Pathology* [*Arch. Path. (Chicago)*] **59**, 269–284, March, 1955. 21 figs., bibliography.

The literature on carbon tetrachloride poisoning, expecially from U.S. sources, is already extensive, but there is still a need for critical study of the histological changes in the liver and kidney in fatal cases. The clinical and pathological findings in a series of 8 such cases are here reported from the Northwestern University Medical School, Chicago, 3 of the patients having died 9 to 12 days after exposure from renal failure, one 2 hours after exposure from the anaesthetic effects of carbon tetrachloride, and the remaining 4 forming a distinct clinical group in which death occurred within 96 hours of exposure after a fulminating course, there having been no signs of renal failure. In this last type of case, which does not appear to have been described previously, death was due to hepatic failure, and the histological changes were confined to the liver and kidney. In the liver centrilobular necrosis and fat infiltration were diffusely distributed, very little parenchyma remaining, and the kidneys showed a histological picture of fat nephrosis resembling that of " lower nephron nephrosis ". [These intermediate renal changes have, of course, been widely described, notably by Woods.]

It would appear that those patients who do not immediately succumb to the narcotic effects of carbon tetrachloride die rapidly of hepatic failure or, if they survive this, suffer varying degrees of " lower nephron nephrosis ". The close similarity between the hepatic and renal lesions of carbon tetrachloride poisoning and of those due to phosphorus, chloral hydrate, tetrachlorethane, and other chlorinated hydrocarbons will be of particular interest to toxicologists. *Keith Simpson*

1152. **Multiple Toxic Effects of Phenylbutazone. Report of a Fatal Case**
T. N. FRASER. *British Medical Journal* [*Brit. med. J.*] **1**, 1318–1320, May 28, 1955. 28 refs.

1153. **A General Survey of Toxicological Investigations for Arsenic. The Value of Examination of the Hair.** (Données générales sur la recherche de l'arsenic en toxicologie. Intérêt de l'examen des cheveux)
M. H. GRIFFON. *Annales pharmaceutiques françaises* [*Ann. pharm. franç.*] **13**, 258–283, April, 1955. 2 figs., 33 refs.

Anaesthetics

1154. **New Short-acting Thiobarbiturate**
P. NOBES. *Lancet* [*Lancet*] **1**, 797–799, April 16, 1955. 2 refs.

Whereas barbiturates like hexobarbitone and sodium thiopentone are apt to cause somnolence after operation, a new short-acting drug, " baytenal " (5:5-allyl-(2-methylpropyl)-thiobarbiturate) is eliminated from the body so rapidly that there is little, if any, postoperative somnolence. At Chase Farm Hospital, Enfield, Middlesex, baytenal was given by injection to the author in an initial dose of 0·6 g. followed by 0·4 g. 1½ minutes later; 6 minutes after the initial injection full consciousness returned. The drug was also given to 11 patients; recovery was rapid, there were no after-effects, and respiratory depression was very slight.

W. Stanley Sykes

1155. **The Effects of Nisentil Hydrochloride and Levallorphan Tartrate on Cerebrospinal Fluid Pressure**
M. SWERDLOW, F. F. FOLDES, and E. S. SIKER. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **27**, 244–249, May, 1955. 1 fig., 10 refs.

1156. **Pulmonary Ventilation during Anaesthesia. A Comparison between Spontaneous and Artificial Respiration with Thiopentone, Gallamine Triethiodide and Pethidine**
A. B. EASTWOOD and R. P. HARBORD. *Anaesthesia* [*Anaesthesia*] **10**, 34–45, Jan., 1955. 6 figs., 6 refs.

This study was undertaken at the University of Leeds in an attempt to correlate measured changes in spontaneous and artificial respiratory tidal volume with those of alveolar carbon dioxide concentration in man during thiopentone anaesthesia. The subjects chosen for study were 44 healthy individuals (average age 42 years) undergoing relatively minor surgical operations. Premedication was by standard methods and induction of anaesthesia was with thiopentone, gallamine triethiodide, and oxygen, a cuffed tube and soda-lime absorber being employed. Measurement of spontaneous respiratory rates and volumes was by means of a spirometer substituted for the rebreathing bag; for measurement of controlled inflation rates and volumes in apnoeic patients an apparatus embodying a bellows for inflation of the patient and with a valve by means of which the whole of each expiration passed into the spirometer was substituted. Gas samples at the end of forced expiration were collected in sampling tubes and estimated in a Haldane apparatus.

Of 68 estimations made during spontaneous respiration, 17 showed a carbon dioxide content of 4·7 to 6·4% and 4 a figure less than 4·7%, but in the majority (47) it was between 6·4 and 9·8%. The respiratory rates ranged from below 14 (7 cases) to 28 per minute. Of 33 estimations made during artificial respiration, 25 showed a carbon dioxide concentration of 4·7 to 6·4%, one was less than 4·7%, and 7 showed a concentration greater than 6·4%; of these last, 5 had a tidal volume of over 350 ml.

These results are discussed in relation to the findings of other workers.

B. L. Finer

1157. **Hypothermia: Some Observations on Blood Gas and Electrolyte Changes during Surface Cooling**
I. K. R. MCMILLAN, D. G. MELROSE, and R. B. LYNN. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **16**, 186–194, March, 1955. 5 figs., 14 refs.

One of the main hazards encountered in carrying out hypothermic techniques is the occurrence of ventricular fibrillation, but the factors implicated in its causation are still not well understood. The authors, working at the Buckston Browne Research Farm, Downe, Kent, have investigated the relation of the blood carbon dioxide concentration and changes in plasma electrolyte content to the incidence of ventricular fibrillation in 28 dogs, which were cooled by immersion in iced water. They were divided into two groups: Group 1 contained 14 dogs breathing spontaneously, of which 5 were anaesthetized with intraperitoneal " nembutal " (pentobarbitone sodium) and a cuffed tube passed, while 9, after premedication with 0·6 mg. of atropine, were anaesthetized with intravenous sodium thiopentone given in divided doses as required to maintain anaesthesia and prevent shivering; a cuffed tube was passed and oxygen was breathed spontaneously, a carbon dioxide absorber being inserted in the circuit. Group 2 consisted of 12 dogs in which respiration was controlled. The anaesthetic technique was as before, but 9 of the animals were paralysed with curare or succinylcholine and connected to an automatic positive–negative-pressure respirator, a carbon dioxide absorber again being in every circuit. Blood pressure was measured by means of a cannula in the femoral artery, from which also blood samples for determination of oxygen and CO_2 concentration and electrolyte levels were withdrawn. Body temperature was measured by thermometers in the mid-thoracic oesophagus and rectum.

In animals in Group 1 the arterial CO_2 concentration rose and the *p*H fell; the plasma levels of total, free, and bound calcium all rose, whereas the plasma sodium, potassium, and magnesium levels showed little over-all change. In those in Group 2 the arterial CO_2 concentration fell and the *p*H rose; the plasma total and free calcium levels rose, but less than in Group 1, while the bound calcium value fell slightly. The calcium:potassium ratio rose more in Group 1 than in Group 2. In 9 of the animals the arterial oxygen saturation and arterio-venous oxygen difference remained within the normal range. All values, which are given in detail and

also illustrated graphically, returned to normal on rewarming.

The authors conclude that there are many factors concerned in the development of ventricular fibrillation, the most suggestive factor which emerged from this study being the rise in the calcium:potassium ratio.

B. L. Finer

1158. **Some Circulatory Aspects of Induced Hypotension with Hexamethonium**

J. A. GRIFFITHS. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **27**, 211–228, May, 1955. 11 figs., 30 refs.

The author describes investigations carried out at the United Sheffield Hospitals into some of the circulatory aspects of induced hypotension.

The bleeding time was estimated by a modification of Ivy's technique during anaesthesia by a standard method in 100 cases, in 50 of which the blood pressure was reduced by means of hexamethonium to levels between 65 and 80 mm. Hg. It was found that while both groups showed some slight increase in the bleeding time (which was normal before operation in all cases), there was no significant difference between them. The author draws attention to the need for careful ligation of all severed vessels, whether bleeding or not, during operations under hypotension if reactionary haemorrhage is to be avoided.

In 40 cases the effect of anaesthesia and of induced hypotension on the circulation time, as estimated with "cardophyllin" (theophylline–ethylenediamine) by the method of Koster and Sarnoff (*J. Lab. clin. Med.*, 1943, **28**, 812) was studied, the end-point being recorded on a spirometer. There was no increase in the arm–respiratory-centre circulation time after induction of anaesthesia, but an increase was observed after induction of hypotension, the increase showing no quantitative correlation, however, with the degree of hypotension. The circulation time from the ankle, but not that from the arm, was prolonged by increasing the foot-down tilt from 5 to 15 degrees.

The blood pressure was recorded during induced hypotension in 5 cases by intra-arterial capacitance manometry and the accuracy of readings obtained by auscultation with a mercury sphygmomanometer checked. It was found that the point of disappearance of the sound corresponded better with the diastolic pressure as measured directly than did the point of "muffling" of the sound, and that with careful use the sphygmomanometer gave a sufficiently reliable indication of the systolic pressure between 60 and 80 mm. Hg. The author describes observations suggesting that underfilling of the arterial system does not occur until the systolic pressure falls below 65 mm. Hg.

After operation posture should be strictly regulated until normal vasomotor control has been regained. It is emphasized that the use of pressor agents to raise the blood pressure does not reverse the ganglionic blockade by hexamethonium, so that vasomotor control is still diminished in such circumstances; it is also reduced by analgesics such as morphine and pethidine.

Certain pressor responses remain unaffected after the induction of hypotension with hexamethonium. For example, manipulation of the adrenal glands in 2 cases produced a severe rise in blood pressure, exaggerated by the removal of the normal compensatory mechanisms by the hexamethonium. In another case a pressor response occurred to acute anoxia; the mode of its production is discussed and it is concluded that it was probably caused by direct stimulation of the adrenal glands, as evidenced by an accompanying tachycardia and rise in blood sugar level.

Raymond Vale

1159. **Renal Circulation during Anaesthesia and Surgery**

H. E. DE WARDENER. *Anaesthesia* [*Anaesthesia*] **10**, 18–33, Jan., 1955. 12 figs., 18 refs.

Acute renal failure, apart from that due to nephrotoxic substances such as mercury, is usually caused by intense renal ischaemia. To clarify the causes of acute post-operative renal failure the author, working at St. Thomas's Hospital, London, has studied the renal blood flow during surgical anaesthesia, first in a group of healthy young males undergoing operations for varicose veins or herniorrhaphy, since these minor operations are known to have no effect on renal blood flow. The renal blood flow was calculated from the renal plasma flow, determined by PAH clearance, and from the venous haematocrit value. Anaesthesia, which was either very light or very deep, was by ether or cyclopropane in a closed circuit with 100% oxygen, controlled respiration being carried out during deep anaesthesia.

The author's observations showed that during anaesthesia the renal blood flow was markedly reduced, the more so as anaesthesia deepened, but the duration of anaesthesia had no direct effect and recovery to a normal level of blood flow was rapid when anaesthesia was discontinued. Animal experiments carried out on dogs suggested that this renal vasoconstriction was of neurogenic origin. In another group of patients undergoing partial gastrectomy and cholecystectomy it was found that the renal blood flow was not affected, but traction on the large bowel in one case produced complete renal ischaemia for one hour.

In a study of the effect of hypotensive and hypertensive drugs the induction with of pentamethonium bromide of hypotension in young healthy adults under cyclopropane or ether anaesthesia produced no change in the renal blood flow or in the incidence of postoperative renal complications. When noradrenaline and adrenaline were given, however, the renal blood flow decreased, whereas methylamphetamine caused an increase in 5 out of 6 subjects. Lastly, a study of the effects of haemorrhage showed that a loss of 800 to 1,500 ml. of blood during anaesthesia produced no significant change in renal plasma flow or heart rate during the following hour.

The author concludes that the combination of post-operative renal vasoconstriction and hypotension resulting from under-estimated haemorrhage during operation is one of the most likely causes of tubular necrosis and acute renal failure following surgical operations.

B. L. Finer

See also Pathology, Abstract 920.

Radiology

RADIODIAGNOSIS

1160. **Preliminary Report on the Use of Contrast Media in Orbital Radiography**
J. W. COWIE and J. S. GROVES. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **39**, 283–293, May, 1955. 10 figs., 18 refs.

In this paper from the General Infirmary at Leeds the authors discuss the use of contrast media in orbital radiography and describe a technique for the injection of diodone—the medium of choice—into the various tissue spaces of the orbit. The episcleral space and the muscle cone (central surgical space) can be easily identified and their displacement estimated; the vitreous cavity can also be outlined. The results obtained with this technique in 4 patients with orbital tumour are described. The authors consider that the method is safe and worthy of further trial. *A. G. Cross*

1161. **Enlargement Radiography of the Petrous Bone in Osteitis Deformans (Paget's Disease).** (La radiographie agrandie du rocher dans l'ostéite déformante de Paget)
M. JUSTER, J. MICHEL, H. FISCHGOLD, and J. A. LIÈVRE. *Presse médicale* [*Presse méd.*] **63**, 308–311, March 2, 1955. 8 figs., 7 refs.

Preliminary radiographs were made of sections of dried temporal bone varying in thickness from 1 to 10 mm. by an enlargement technique, a fine-focus *x*-ray tube with a target 0·3 mm. in diameter being employed, giving a magnification of ×2 to ×2·2. The technique was then applied to examination of the petrous bone in 24 confirmed cases of Paget's disease. The method, which was fully described by Layani and Fischgold (*Presse méd.*, 1953, **61**, 279), gives considerably more information than does normal radiography.

In the petrous bones examined there was progressive resorption of the cortex and compact bone surrounding the labyrinth and internal auditory canal, and at the tip of the petrous the compact bone was separated by cracks which in some cases enlarged into cavities. In only 3 out of the 24 specimens examined were the petrous bones normal; in the others the following lesions were observed. (1) Damage to the cortex of the superior border varying from a simple thinning to complete disappearance. (2) Damage to the cancellous bone, consisting in a reduction in the thickness and number of the trabeculations; in one case, however, there was increased density of the petrous. (3) An increased visibility of the internal auditory organs; in the case with increased density of the petrous, however, these organs were less visible than usual. (4) Disappearance to a greater or less extent of the dense bone surrounding the inner ear was seen in 14 cases, in some being confined to either the cochlea or the labyrinth. In more than half the cases the changes were bilateral and symmetrical.

There appeared to be no direct relation between the extracranial changes and those in the petrous bone, but there was a close relationship between the other changes in the skull and those in the petrous. While changes in the petrous bone were always present when there were significant changes in other parts of the skull, in 3 cases the petrous changes were the only ones present. Of the 24 patients, 15 had deafness of some degree, the degree of deafness being directly correlated with the radiological changes, so that those cases with the most marked radiological changes showed the most severe changes in the inner ear. *John H. L. Conway-Hughes*

1162. **Routine Preoperative Chest Radiography. Analysis of 1,000 Cases**
R. E. LODER. *Lancet* [*Lancet*] **1**, 1150, June 4, 1955. 2 refs.

1163. **On the Recognition and Significance of Pleural Lymphatic Dilatation**
B. LEVIN. *American Heart Journal* [*Amer. Heart J.*] **49**, 521–537, April, 1955. 7 figs., 12 refs.

The postero-anterior chest radiographs of patients suffering from mitral stenosis not uncommonly show short, narrow, transverse lines towards the periphery of the basal lung fields. These appearances, which were the subject of the study here reported from the University of Minnesota Hospitals, Minneapolis, have been studied previously by a number of workers and their association with pulmonary hypertension has been noted, but their exact significance has not been fully understood.

After briefly considering the lymphatic system of the lungs the author suggests that the horizontal linear shadows are due to dilated interlobular lymphatic channels which extend outward to join the pleural plexus of lymphatics at right angles, and gives his reasons for discounting other causes, such as basal emphysema and atelectasis. These views are based on the investigation of 63 patients with mitral stenosis, each of whom had been studied by right heart catheterization, the pulmonary arterial pressure being measured in all cases, and the pulmonary wedge pressure in 27. In the chest radiographs of 39 of these patients the typical transverse basal striae were demonstrable, and a positive correlation was found between the degree of basal pulmonary striation and the pulmonary arterial and wedge pressures.

In addition to the cases of mitral stenosis, a review was also made of the chest radiographs in 20 cases of congenital heart disease with marked pulmonary hypertension, 50 cases showing increased blood flow through the pulmonary circuit, and 23 cases in men with left ventricular failure. No basal striae were present in the radiographs in any of these cases, and only 2 out of 300 cases of hypertensive heart disease showed faint striae.

Lastly, a study of the chest radiographs of 30 patients with hypoproteinaemia revealed 2 cases showing basal striae together with pulmonary alveolar oedema; in both these cases the patients were suffering from chronic glomerulonephritis and systemic arterial hypertension.

The pathology and physiology of the condition are discussed. It is considered that the main factor in the production of the striae is a sustained elevated left atrial pressure, eventually leading to pulmonary venous and capillary hypertension. It was noted that the basal striae cleared or diminished in some of the patients after the performance of mitral valvotomy.

[This article forms an interesting and valuable contribution to the study of mitral stenosis.]

Sydney J. Hinds

1164. **A Critical Evaluation of the Roentgen Criteria of Right Ventricular Enlargement**

M. L. SUSSMAN and G. JACOBSON. *Circulation* [*Circulation (N.Y.)*] **11**, 391–399, March, 1955. 3 refs.

From a study of 40 cases of congenital pulmonary stenosis and 25 cases of the tetralogy of Fallot in children and young adults the authors demonstrate that reliable evidence of enlargement of the right ventricle cannot be obtained from plain radiographs. No measurements were used, the presence or absence of enlargement being assessed subjectively by two observers. No correlation was found between the right ventricular pressure and the size of the chamber as judged by this method.

G. Simon

1165. **Benign and Malignant Gastric Ulcers: Roentgen Differentiation**

I. E. KIRSH. *Radiology* [*Radiology*] **64**, 357–365, March, 1955. 3 figs., 29 refs.

Among 24,000 cases in which radiological examinations of the gastro-intestinal tract were carried out at the Veterans Administration Hospital, Hines, Illinois, over a 5-year period there were 209 cases of proved gastric carcinoma. The radiographs in 22 of these cases in which the lesion was "predominantly ulcerative" were compared with those in 120 cases of simple gastric ulcer seen during the same period and subsequently verified histologically. Radiating folds which could be followed to the very edge of the crater were observed in 50 of the cases of simple ulcer but in none of the cases of malignant ulcer. The author states that if such folds are seen in the vicinity of the crater but are broken off immediately around it, malignancy should be suspected. Other findings were a filling defect, in 19 of the 22 cases, and abnormal folds near the base of the crater, also in 19 cases; however, the former sign was present in 17 of the 118 cases of benign ulcer and the latter in 15, and the author points out that although they are important, they should not be considered pathognomonic of carcinoma. The site of the ulcer and its size were found to be of little diagnostic value. The base of the crater was irregular in 7 cases of malignant and in 21 of benign ulcer. A lobulated base in a case of simple ulcer usually meant penetration into the pancreas. Gastric retention (for 5 to 6 hours) occurred in about half the cases in both groups.

The diagnoses on radiological examination and at gastroscopy are compared as follows:

Finding	Histologically Benign		Histologically Malignant	
	X-ray examination	Gastroscopy	*X*-ray examination	Gastroscopy
"Benign"	99	33	9	1
"?Malignant" ..	4	14	7	0
"Malignant" ..	11	4	6	10
Poor view and no diagnosis ..	—	5	—	1
No lesion found ..	6	—	—	—
Lesion not seen ..	—	26	—	5
No examination ..	—	38	—	5
Total ..	120	120	22	22

[The useful diagnosis which leads to long-term survival is more difficult to make than this paper would suggest. There is no mention of the hardest diagnostic problem—that of the carcinoma which many histologists still describe as "arising on the edge of a simple ulcer".]

Denys Jennings

1166. **Pancreatography. Technics, Principles, and Observations**

H. DOUBILET, M. H. POPPEL, and J. H. MULHOLLAND. *Radiology* [*Radiology*] **64**, 325–339, March, 1955. 55 figs., 5 refs.

Pancreatography may be carried out at operation by transduodenal section of the sphincter of Oddi and the insertion of a plastic tube into the main pancreatic duct, 10 ml. of 70% diodone being then introduced over a 5-minute period. Moreover, since the pancreatic duct is often dilated in cases of long-standing pancreatitis the therapeutic effect of postoperative drainage has been tried, a polyvinyl tube 1·3 to 1·7 mm. in diameter being inserted up the duct of Wirsung for 4 to 5 cm. and then brought out through the duodenum and common bile duct alongside the rubber T tube in cases in which the common bile duct has been drained; otherwise the plastic tube is brought out through the cystic duct. Such a pancreatic fistula can be maintained for weeks or months and allows serial pancreatography to be carried out, the patient, who must be in the fasting state, being given 15 mg. of propantheline ("probanthine") intramuscularly an hour before each examination.

The present authors, working at New York University College of Medicine, have found pancreatography to be of diagnostic value, 201 observations having been made on 100 patients. Blockage of the duct system was often observed, but the most interesting discovery was that in acute inflammation the ductal epithelium becomes permeable to the medium so that the whole gland, or a localized area of inflammation within it, becomes diffusely opacified, the opacification becoming less with recovery. The authors point out that this increased permeability explains the rise in the serum amylase and lipase levels which can occur in cases of obstruction of the pancreatic duct even while the pressure in the intraductal system is falling. Diodone acts as an irritant, so that if a second injection is given after 10 minutes

even the normal pancreas is opacified. Since adenomata of the pancreas are not connected with the duct system such a procedure should, in theory, be useful in their detection. However, no success was obtained with this technique in a patient with hyperinsulinism in whom an adenoma could not be palpated at operation.

[The incidence of pain and complications is not discussed.] *Denys Jennings*

1167. **Translumbar Aortography as a Diagnostic Procedure in Urology. With Notes on Caval Phlebography** N. S. R. MALUF and C. B. MCCOY. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **73**, 533–573, April, 1955. 74 figs., bibliography.

The authors, from the Columbia–Presbyterian Hospital, New York, discuss their experience of translumbar aortography as a diagnostic procedure in urology, with special reference to their findings in some 250 cases. Local analgesia has been found to be preferable to general or spinal anaesthesia, and 70% "urokon" the most suitable contrast medium. The examination is usually carried out in the early afternoon, the patient having fasted since 9 a.m. and having received 200 mg. of phenobarbitone intravenously at noon. After the patient is centred in the prone position 0·25 ml. of the contrast medium is injected intravenously followed by 100 mg. of pethidine. The area caudal to the 12th left rib is infiltrated with analgesic. A No. 17-gauge needle with a 16-gauge lumen, a 15-cm. shaft, and a short bevel is inserted a hand's breadth to the left of the spinous processes and immediately caudal to the 12th rib at an angle of 45 degrees. When the needle is judged to be 2 to 3 cm. from the aorta a preliminary radiograph is taken. The aorta should be entered at the level of T12, where it is free from branches. Initially, 2 ml. of the contrast medium is introduced; if there is no extravasation the remainder of the 20 to 40 ml. is given as quickly as possible, the radiograph being taken while the last 5 ml. is being injected. After the patient returns to the ward pulse rate and blood pressure are recorded half-hourly for 5 hours, and if these are normal the patient is allowed to return home. Advanced age is not a contraindication to this procedure, but it is not advocated in children under 10 years. Caval phlebography is used to demonstrate involvement of the inferior vena cava by renal or adrenal neoplasms and also patency of a portacaval anastomosis. The venous return from the legs is occluded by Esmarch bandages and 40 ml. of opaque medium is injected rapidly into the femoral vein.

Discussing complications the authors state that laryngeal spasm occurred in some of the cases in their series in which thiopentone was the anaesthetic. Extravasation with local pain was observed in a few cases, but absorption was rapid. In one patient with only 11 ribs bilaterally the aorta was entered within the costovertebral pleural reflection; pleuritis developed, which lasted a few weeks. Severance of the thoracic lymph duct occurred in one case.

In conclusion the authors state that aortography can be of great help in differentiating a renal adenocarcinoma from a renal cyst. "By showing the position and course of the renal artery it indicates the readiest approach to the renal pedicle." Further, an aberrant renal artery and the amount of kidney supplied by such an artery, as well as the presence or absence of a kidney, can be demonstrated by this procedure.

John H. L. Conway-Hughes

RADIOTHERAPY

1168. **Simple Mastectomy and Radiotherapy in the Treatment of Breast Cancer** R. MCWHIRTER. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 128–139, March, 1955. 4 figs., 6 refs.

Doubts about the value of radiotherapy as an adjuvant to surgery in the treatment of cancer of the breast have been aroused (1) because a few surgeons have reported high survival rates from surgery alone, omitting to make clear that their cases were highly selected, and (2) because it is not always realized that there are great differences in the technique of applying *x* rays, so that the treatment actually given may have been of no value. Throughout this paper from the Royal Infirmary, Edinburgh, the author stresses the importance of basing survival rates on *all* cases of breast cancer referred to a hospital, and not on highly selected groups of cases chosen mainly on the grounds of operability.

The mode of spread of cancer of the breast is outlined in detail, since on this depends the treatment policy of simple or radical mastectomy and postoperative radiotherapy. The lymph nodes of the axilla and supraclavicular fossa form one continuous chain, for in one-third of operable cases the nodes in the latter site are also involved. The two regions should therefore be irradiated in continuity by the use of two opposed fields. Radical mastectomy fails to deal with spread to the mediastinum, so the surgeon relies upon the radiotherapist to irradiate the mediastinum and supraclavicular nodes. In the author's opinion he should extend his faith farther and allow the radiologist to sterilize the axillary nodes also, for these nodes are equally as radiosensitive as the primary tumour. A dose level of 3,750 r is needed to achieve this. When the disease is strictly confined to the breast a simple mastectomy is as effective as the radical operation. The reasons for considering preoperative radiotherapy are outlined and countered by equally good reasons for giving it postoperatively.

A total of 1,882 cases which were recorded and treated in the period 1941–7 are here analysed in three groups: operable cases, locally advanced cases, and cases with distant metastases. In calculating survival rates it was assumed that all deaths were due to malignant disease, and rather than make corrections for deaths from intercurrent disease an age limit of 60 years was arbitrarily set in determining the 10-year survival rate and one of 65 years for the 5-year survival rate, since the patient's age is important in considering life expectancy. The 5-year crude survival rate was as follows: operable cases 58%, locally advanced cases 30%, and cases with distant metastases 4%, giving an over-all average of 42%; for 10-year survival the corresponding

figures were: 39%, 15%, *nil*; average 25%. Tables are also given showing survival rates in relation to age of the patient and stage, type, and site of the tumour. In arriving at these figures every effort was made to include all cases of breast cancer occurring in south-east Scotland and more than 40 surgeons cooperated in the investigation.

[This is an important paper. The results are clearly set out in detail, and demand the attention and thought of all concerned in the treatment of cancer of the breast.]

R. J. M. Whittle

1169. **Focal Intracavitary Irradiation with Radioactive Thulium.** (Gezielte intrakavitäre Bestrahlung mit Radiothulium)

H. Heuwieser and W. Horst. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **82**, 513–518, April, 1955. 8 figs., 8 refs.

Intracavitary irradiation of the bladder, notably by means of radioactive cobalt, has the disadvantage of treating the whole of the mucosa, normal and abnormal, and thus involves the serious risk of causing severe cystitis, which is the great drawback to such therapy. The only way of localizing the dose to a selected part of the bladder would be by metal screens, but with cobalt impossibly thick screens would be needed because of the penetrating gamma rays which it emits. A weaker ray is therefore needed, and for the studies here reported from the University Hospital, Hamburg–Eppendorf, radioactive thulium (^{170}Tm) was chosen. This emits gamma rays at only 0·084 MeV, and beta rays at 0·97 MeV. A cylindrical source 2 mm. in diameter and 2 mm. long, with an activity of 100 millicuries, was used. The authors point out that a 3-mm. source, with maximum irradiation in the atomic pile, would have a specific activity 80 times as high and provide 350 r per hour at 3 cm. in water, with 50% depth dose at 1 cm. below the mucosa.

The cylinder can be inserted easily in a balloon catheter, even through the male urethra. Lead screens in varying arrangements concentrate the beam on the base, roof, or equator of the bladder. Further limitation of the field can be achieved by screening one side of the thulium source with copper foil, which cuts off 45% of the rays, or with gold foil, which cuts off 95%, thus confining irradiation to one side of the bladder only.

J. Walter

1170. **Value of Preoperative Radiation in Reduction in Size of Single and Multiple Papillary Bladder Tumors**

D. R. Higbee. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **73**, 498–501, March, 1955. 3 figs.

Transurethral fulguration is the treatment of choice in approximately 65% of cases of papillary tumour of the bladder, and statistics indicate that the cure rate is exceptionally high. The present author states that preoperative radiation in selected cases will reduce the size of the tumour sufficiently to make transurethral treatment the method of choice in a larger number of cases, thus avoiding the risks of open surgery while maintaining the high cure rate. It is particularly suitable in cases of moderate-sized tumours lying close to or involving a ureteric orifice, in cases of multiple tumours, and in patients who are unfit for surgery.

The author has employed this method in 30 cases, using high-voltage *x* rays to irradiate the bladder and giving a tumour dose of about 2,500 r through multiple ports over a period of approximately two weeks. Elderly or debilitated patients or those who, for other reasons, did not tolerate radiotherapy well were treated with radium, usually placed in a Foley catheter, the dose being 1,200 to 2,000 mc. hours. The tumour regressed in size over a period of 4 to 6 weeks; cystitis, if it developed, was controlled by administration of antibiotics, but the author states that neither haemorrhage nor cystitis proved troublesome. If there is a recurrence further fulguration or more radical surgery can be carried out, but the author claims that the latter is rarely necessary.

G. E. Flatman

1171. **Experience with Implantation of Radon Seeds for Bladder Tumors: Comparison of Results with Other Forms of Treatment**

J. L. Emmett and J. R. Winterringer. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **73**, 502–515, March, 1955. 33 refs.

The records at the Mayo Clinic of 118 cases of bladder tumour in which radon therapy was given between January, 1935, and December, 1948, were studied. In 89 cases the radon seeds were implanted cystoscopically and in 29 by open operation. In 82 cases some other form of treatment—partial removal of the tumour or fulguration—was carried out in addition, and in 64 deep *x*-ray therapy was also given. While 55 of the 118 patients did not survive the first year after treatment, 33 survived 5 years or more after it. In most cases from 6 to 20 seeds, between 1 and 1·6 millicuries each, were implanted 0·25 cm. to 1 cm. apart into the bladder wall to a depth of about 0·75 to 1 cm. Deep *x*-ray therapy was given concurrently in some cases while in others it was given over a period of 3 months before or after implantation, the tumour dose varying from 1,200 to 6,000 r. Post-irradiation cystitis was not a serious complication, and the authors found that the size and situation of the tumour did not appear to influence the results.

A review of current literature on methods of treatment of bladder tumours shows that the degree of infiltration of the tumour is the most important single factor in survival, although size and location of the tumour, grade of malignancy, and the presence or absence of ureteric obstruction are also important. The proportion of patients surviving 5 years after partial or total cystectomy appears to be approximately 30%, the results of the former operation being superior to those of the latter.

From their findings in the present investigation the authors suggest that implantation of radon, combined if necessary with transurethral removal of the tumour, merits more frequent use than it has been accorded in the past.

G. E. Flatman

See also Dermatology, Abstract 1110.

History of Medicine

1172. **Isaac Buxton, 1773–1825**
N. H. SCHUSTER. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 326–328, April, 1955. 3 figs.

Isaac Buxton was the founder of the Royal Chest Hospital, London, probably the first chest hospital in the world. He was born on May 6, 1773, in Bermondsey, educated at St. Paul's School, and apprenticed for 5 years to his brother-in-law, a seed merchant. Little is known about him during the period 1790 to 1800 except for a report in the *Authentic Memoirs of the Royal College of Physicians* (1818) that he practised as a dissenting minister; the present author, however, was unable to confirm this from Nonconformist records. In 1800 he began the study of medicine at Göttingen under Blumenbach, and obtained his doctorate in 1802, his thesis being apparently a study of man as a ruminant. He returned to London in the same year and enrolled at Guy's Hospital as a pupil dresser to Astley Cooper; in 1805 he obtained the Licence of the Royal College of Physicians. A year later Buxton was appointed to the staff of the Surrey Dispensary and a year later still, in 1807, to the London Hospital. The author refutes the attacks made on Buxton in Morris's *History of the London Hospital* (1910), which attributes his appointment to the London Hospital to "a trick" and his resignation in 1822 to scandal. Morris's statement that Buxton did not belong to the family of that name associated with the London Hospital is also denied. Buxton built up a successful practice in New Broad Street, and was elected to the Council of the Hunterian Society. He died in Camberwell in 1825.

Despite his relative obscurity Buxton has three claims to distinction. (1) In 1810 he published an essay on the heating and ventilation of sick rooms which included a survey of heating systems. He aimed at a constant temperature of 60° to 65° F. (15·5° to 18·3° C.) during winter months for patients with chest complaints. His arguments were supported by statistics and case histories (one supplied by Jenner). (2) After the London fever epidemics of 1817 and 1818 Buxton undertook, on behalf of the London Hospital, a survey of the admissions to that hospital over the previous 70 years. His analysis showed that while the incidence of fever cases had declined over the whole period—a fact attributed to improved standards of hygiene—the mortality was relatively higher because of the reluctance of the authorities to admit cases until the late stage of the disease. This survey is in the library of the Royal College of Physicians. (3) On March 25, 1814, Buxton founded the Infirmary for Asthma, Consumption and other Pulmonary Diseases, later the Royal Chest Hospital, and until 1820 was the sole physician there. The wards were kept at a constant temperature during the winter months, and cases of all chest disorders, including tuberculosis, were admitted. The Infirmary was in Spitalfields for 35 years before it was moved to the City Road. It was damaged by bombs in the air-raids of 1941 and finally closed down in 1954.

F. M. Sutherland

1173. **Dr. John Fryer—an Early Traveller in the East**
D. MCDONALD. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. Med. Hyg.*] **49**, 187–194, March, 1955. 1 fig.

Few of the European doctors who practised in the East during early times have left any personal account of their experiences, and it is therefore particularly interesting to read the detailed descriptions of medical practice and life in India and Persia during the 17th century as recounted by Dr. John Fryer in his *New Account of East India and Persia, being Nine Years Travels, 1672–1681*, which was published in 1698.

Fryer, who was born about 1650, became a surgeon in the service of the East India Company and reached Bombay in December, 1673, exactly a year after leaving England. The discomforts of the voyage and his observations on such conditions as scurvy and elephantiasis are described in some detail in his book, Fryer having a receptive and inquisitive mind, retaining much of the natural curiosity of childhood. In India he industriously collected information of all sorts, notably on the indigenous diseases and methods of treatment, amongst which he mentions the Goa stone, which for centuries, and indeed until last century, was considered a sovereign remedy against mental diseases, all fevers, and poisons. Compounded by the Jesuits of Goa, it contained bezoar stone, coral, gold leaf, and various precious stones such as ruby and pearl. During his travels in India and Persia Fryer met with many adventures and encountered many dangers which are illustrated here by extracts from his book. He returned to England in 1682 but little is known of his subsequent life. He was elected F.R.S. in 1697 and died in 1733.

Douglas Guthrie

1174. **The Work of Benjamin Ward Richardson: Its Effect on Modern Health Practice**
A. S. MACNALTY. *Royal Sanitary Institute Journal* [*Roy. sanit. Inst. J.*] **75**, 201–210, March, 1955. 11 refs.

In this, the Benjamin Ward Richardson Lecture to the Royal Sanitary Institute, London, 1954, the author sums up Richardson's influence on modern public health practice. Richardson began his medical career as an apprentice, but eventually qualified in Glasgow in 1850, taking the degrees of M.A. and M.D. at St. Andrews University four years later. He became F.R.C.P. in 1865, and in 1867 was elected a Fellow of the Royal Society. He received many awards and honours during his lifetime, and was knighted in 1893. His early interests included cholera, toxicology (he gave evidence at the Palmer and Smethurst poison trials), resuscitation, lethal gases, and anaesthetics; he was a pioneer of blood trans-

fusion, and was the first to describe the action of amyl nitrite on the circulation and the therapeutic value of hydrogen peroxide. His writings covered an equally wide field and included biographies of some 46 medical and scientific workers published under the title *Disciples of Aesculapius*, a historical novel, and an autobiography. Late in life he unsuccessfully contested an election for a seat in Parliament.

Richardson's greatest contributions to medicine probably lay in the fields of epidemiology, hygiene, and social medicine, and the publicity he gave to these subjects. "We suffer from disease through ignorance; we escape through knowledge" was a creed he pursued in a number of journals, including the *Sanitary Review* and *Social Science Review*, which he founded. He was an early advocate of the "registration" of diseases and the establishment of a Ministry of Health (this was in 1878), and an ardent promoter of societies for sanitary reform. He was the first chairman of the Sanitary Institute—later the R.S.I.—and helped to establish the Institute's annual congress and the examinations for sanitary inspectors. Tuberculosis, mental health, nutrition, and the humane slaughter of animals were among other subjects to which he gave his attention. It is of interest to note that, although in his early days he was regarded as a connoisseur of wines and was a constant pipe smoker, he later became a temperance reformer and abstained from smoking. He died from cerebral haemorrhage.

[The author has given a fascinating picture of a fascinating man; could anyone successfully engage in Richardson's many and catholic activities to-day?]

R. J. Matthews

1175. **William Clift, F.R.S., First Conservator of the Hunterian Museum**

J. Dobson. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 323–325, April, 1955.

William Clift, the son of a miller, was born at Burford Mill, near Bodmin, Cornwall, on February 14, 1775. He showed great promise at school, and although the family was poor after his father's early death, he was kept there until his mother died in 1786. Some years of casual work followed until 1792 when, on the recommendation of the wife of a local landowner, Mrs. Gilbert, who had been at school with John Hunter's wife, he became amanuensis to Hunter at 28, Leicester Square, London, living with Hunter's resident pupils. His daily routine with his master included dissection and preparation of specimens for the museum, keeping visiting and engagement lists, attending drawing lessons, answering correspondence, arranging new descriptions for the catalogue, and recording cases. The harmony between Hunter and Clift was such that, after the former's sudden death in 1793, Clift alone realized the importance of the museum to Hunter and the need for its ordered arrangement to be undisturbed. He cared for it so well that its quality was unimpaired when it was bought by the Government in 1799 and given into the care of the new Royal College of Surgeons.

Clift was appointed Conservator and in 1806 supervised the removal of the museum from Castle Street to the College's new building in Lincoln's Inn Fields, where he and his family took up residence. His duties, apart from those of general care of the museum, included dissection of executed criminals, one of whom was John Bellingham who assassinated Spencer Perceval, the Prime Minister, in 1812. Clift's interests were wide; he taught himself French and German and built up a library of scientific and other works; he attended meetings of the Anatomical, the Geological, and the Zoological Societies, and acquainted himself with the progress of the arts in general.

In 1823 Clift's son was appointed Assistant Conservator and he himself was elected a Fellow of the Royal Society. In the same year Everard Home burnt Hunter's manuscripts, and the value of Clift's copies of Hunter's notes became apparent. After the death of Clift's son as the result of an accident in 1832, Richard Owen, who had been appointed an Assistant Conservator in 1827, gradually began to take over the heavier duties in the museum. In 1834, the need for more space having become urgent, the museum was closed for reconstruction; it was reopened in 1837. Clift retired in favour of Owen in 1842 and lived in Regent's Park until his death in 1849. His finest virtues were loyalty and courage, and his lasting achievement was the preservation of Hunter's museum in its original order.

F. M. Sutherland

1176. **The Prostheses of Ambroise Paré**

T. Gibson. *British Journal of Plastic Surgery* [*Brit. J. plast. Surg.*] **8**, 3–8, April, 1955. 11 figs.

An account is given, with illustrations, of some of the prostheses designed by Ambroise Paré and described in his writings, the first complete edition of which appeared in 1575. Paré's illustrations show examples of practically all the external prostheses which are in use at the present time. He was handicapped in the choice of materials, but he seems to have had a complete understanding of the problems involved in fixation.

His chief external facial prostheses include artificial eyes, noses, and ears, and he was able to devise ingenious palatal obturators to which were affixed retention devices. As a military surgeon during the French campaigns of the middle third of the 16th century he had to deal with amputations not only of limbs, but also of the external genital organs—an artificial penis made of wood or tin is depicted. Paré designed artificial limbs of considerable mechanical ingenuity and, apart from their weight, it is remarkable how closely some of them resemble present-day models.

The paper concludes with this quotation from the 17th volume of the 4th edition of Paré's complete works (1585): "Those who have lost their hair from shock, alopecia or other causes can have a false wig. Also those ladies who have silvered hair for fear of being thought old, may wear artificial fronts of hair which they know well how to arrange and disguise so as often to deceive the men. And also to make themselves appear taller than they are, they wear high heels after the style of Italian and Spanish women".

[This short paper will prove fascinating to those interested in the subject.]

Leon Gillis